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THE IMPORTANCE OF OCULAR SIGNS IN THE DIAGNOSIS OF BRAIN TUMOR*

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ORDINARILY, when discussing the diagnosis of brain tumors, one passes in review more or less completely the whole gamut of diagnostic signs and symptoms. But in this paper I propose to select only one small part of the nervous system—the eyes—and try to show how it may be possible to localize a lesion in almost any part of the brain if the study of this part be sufficiently thorough.

The eyes should be studied from five angles:

I. Ocular palsies.
II. Ocular movements.
III. Visual defects.
IV. Ophthalmoscopic changes.
V. Subjective visual disturbances.

I. Ocular Palsies. The nerve most frequently affected by a brain tumor is the sixth nerve. This is due to the fact that it has such a very long course in the cranial cavity, and also because it may be compressed as it leaves the pons by one of the branches of the basilar artery. As the pressure on the nerve may vary from day to day, or even from hour to hour, the patient's ability to turn the eye outward will also vary. Such a sixth nerve paresis is usually unilateral. It is of no localizing value and must be considered a sign of general pressure.

On the other hand, a bilateral sixth nerve paralysis, inability to look to either side, is of great significance because in my experience it always means a lesion of the medulla where the two sixth nerves have their origin.

When the oculomotor nerve, the third, is thrown out of function, the pupil is dilated, and the eye can be moved only outward and downward. This striking picture, when it occurs suddenly, not only indicates where the lesion is but what it is, namely, an aneurysm of the internal carotid where it enters the circle of Willis. Such cases may have no other symptom

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than headache; the eye grounds remain normal; there is no choked disc. If, however, a third nerve paralysis develops somewhat slowly, and is combined with a choked disc, we must conclude that we are dealing with a tumor in that region, the favorite site of which is just in front of the carotid at the sphenoidal fissure. The tumors at this point have their origin from the meninges and are meningiomas, one of the most satisfactory types of brain tumor which we are called upon to treat. But mere dilatation of the pupil, without any involvement of the other muscles supplied by the third nerve, is of entirely different significance. When that happens, only the sympathetic fibers are involved. One sees this in apoplectic conditions and especially in head injuries. Such dilatation is a grave prognostic sign, and usually means a lesion, most often a hemorrhage, in or near the lateral ventricle of the same side.

II. Ocular Movements. The disturbances of ocular movements are the various types of nystagmus. Lateral nystagmus, when the to and fro movement is equally rapid, may be due to a congenital lesion or to multiple sclerosis; but when there is a rapid component to one side with a slower recovery, then there is a disturbance of the vestibular mechanism; and if the patient has other signs of a tumor we may be quite certain that the nystagmus is caused by an irritative lesion in one of the lateral lobes of the cerebellum,—in the right lobe if the nystagmus is more marked to the right, and in the left lobe if it is more to the left.

Vertical nystagmus is a very different affair. Not only is it produced in quite a different way but it is of considerable prognostic value, which cannot be said of lateral nystagmus. It is a much graver sign than lateral nystagmus because it is produced by an *irritative* lesion far forward in the posterior cranial fossa and is evidence that the lesion, almost invariably a tumor, is pressing upon the corpora quadrigemina. These tumors lie in the median line in the fourth ventricle, and usually are medulloblastomas which are very radio-sensitive. But if a patient is unable to turn his eyes upward, we may be sure that we are dealing with a *destructive* lesion of the corpora quadrigemina and not an irritative lesion of that area. Such lesions, some of them pineal tumors, usually lie in the posterior portion of the third ventricle which but a few years ago was a "noli me tangere" for the neurological surgeon. Today, however, in every large neurosurgical clinic, a number of such tumors have been successfully removed.

As a rule, the absence of a symptom is not of diagnostic value, yet the absence of nystagmus may at times be of very great significance. If a patient presents all the cardinal symptoms of a cerebellar lesion, but has no nystagmus, it means either that the lesion is on the surface of the lateral lobe of the cerebellum and has not involved the nuclei of the cerebellum, or that the lesion is in the region of the middle lobe, the vermis, well away from the lateral cerebellar nuclei which control the lateral eye movements.

I shall merely mention in passing the conjugate movement of the eyes

to one side, which is sometimes confused with nystagmus, but which has its origin in a center in the frontal lobe; and the mistaking of cerebellar tumors for frontal lobe tumors in the past was probably due in part to the misinterpretation of this symptom.

I cannot leave this phase of the subject without drawing attention to unilateral exophthalmos, caused by a meningioma growing from the olfactory groove, which occurs often without any other signs of an intracranial tumor and occasionally in orbito-ethmoidal osteomata. Nor can I omit mention of that extraordinary phenomenon, pulsating exophthalmos, due either to an arteriovenous aneurysm or to a vascular tumor behind the orbit.

III. Visual Defects. The optic nerves and their cerebral connections extend from the under surface of the brain in the anterior fossa to the posterior portion of the middle fossa. Lesions in the course of the visual pathway may produce different kinds of field defects, and by these field defects alone it may be possible to locate a lesion quite accurately. These defects may consist of scotomata, central or paracentral; partial or complete bitemporal hemianopsia; partial or complete homonymous hemianopsia.

A lesion that presses directly on the optic nerve may produce a primary optic atrophy and associated with this a central or paracentral scotoma. A lesion in the orbit or an intracranial lesion in the anterior fossa in front of the chiasm may produce unilateral optic atrophy. If the process has been present for a long time, the patient may lose the sight of one eye completely. We have seen this a number of times in tumors of the pituitary gland. In the series of 78 cases of pituitary tumors and suprasellar cysts which we have operated upon, blindness in one eye occurred 28 times; 18 times in the pituitary tumor cases and 10 times in the cases of suprasellar cysts. There may also be unilateral blindness caused by primary optic atrophy associated with a choked disc in the opposite eye,—that interesting but rather rare syndrome described by Foster Kennedy. This means that there is a lesion on the under surface of the frontal lobe on the side of the optic atrophy. The tumor pressing directly on the nerve causes the atrophy and by causing increased intracranial pressure produces a choked disc in the opposite eye. The eye disturbance associated with a pituitary tumor is practically always a primary optic atrophy. Only in those very rare cases in which a pituitary tumor perforates the dural envelope which roofs the sella turcica, and hence becomes intradural, does one see a choked disc. This has occurred only once or twice in our series.

The characteristic field defect produced by a pituitary tumor is bitemporal hemianopsia and this is unaccompanied by choked disc. In an early case, the bitemporal defect may be detected only in the color fields. A pituitary tumor, however, may grow out to one side and then produce an homonymous hemianopsia. Such a field defect is indistinguishable from that produced by an occipital lobe lesion, but if the tumor is in the occipital

lobe there will almost certainly be double choked disc, while the pituitary case will have only a primary optic atrophy and characteristic roentgen-ray changes in the sella.

I have seen a few cases of hemorrhage into the occipital lobe, apoplexy of the occipital lobe, in which there was no choked disc, but in these cases the history of a sudden vascular insult will enable one to make the differential diagnosis.

Some of the visual fibers, as they pass back toward the cuneus of the occipital lobe, make a loop in the temporal lobe; those fibers which pass to the outer side of the inferior horn of the lateral ventricle control vision in the upper outer quadrant, while those which pass to the mesial side of the ventricle control the lower outer quadrant. The nearer the lesion lies to the occipital lobe, the more nearly complete is the homonymous hemianopsia but the macular, or central vision, in an occipital lobe lesion is spared because the macula is bilaterally represented.

The right temporal lobe, in a right-hand individual, was until recently considered a silent area of the brain, but these partial homonymous defects are so definite and so characteristic that they alone enable one to localize a lesion in the temporal lobe.

To recognize these different types of field defects, it is essential that the examination be carried out with great care. A careless or hastily made perimetric study will not reveal such slight defects and vision must be tested every 15 degrees in order to detect these changes.

Patients with such homonymous field defects often have peculiar subjective visual disturbances—hallucinations. The character of these hallucinations frequently will enable one to differentiate a temporal from an occipital lobe lesion.

IV. Ophthalmoscopic Changes. The ophthalmoscopic study of the eye grounds is another aspect of the ocular mechanism that yields invaluable information. There are two general types of changes that one may observe: First, primary optic atrophy; and second, choked disc or papilledema.

An intracranial, intradural tumor never causes bilateral primary optic atrophy. Consequently, we may conclude that if a patient has other evidence of an intracranial lesion and bilateral primary optic atrophy, the lesion must be extradural. The only intracranial lesions that produce this picture are situated around the chiasm. Most frequently these are pituitary tumors, aneurysms of the internal carotid, or an inflammatory process in that region. But of course it does not follow that because a patient has a primary optic atrophy the lesion is necessarily intracranial, for lesions in the orbit may also cause such atrophy. Since a variety of extracranial causes may produce such a picture, other diagnostic signs have to be taken into consideration before arriving at a final diagnosis.

Choked disc is always due to increased intradural pressure. In the vast majority of cases the pathological lesion is a brain tumor and in these

cases the appearance of the choked disc offers many points of interest. First of all we must ask, can a choked disc be of any localizing value? It has been claimed that unilateral choked disc indicates the side on which the lesion is located. In my experience this is rarely the case, and unilateral choked disc, therefore, is of very little localizing value. Nor are the number of diopters of swelling of much importance. What we must be interested in is the age of the process, and this is best judged by the changes, histological in character, seen with the ophthalmoscope. The character of the hemorrhages, whether recent or old, and the presence of exudate, which is evidence that new tissue is being laid down in the retina, are the points to be looked for. The diopters of swelling, on the other hand, are merely evidence of the amount of edema, and this fluctuates so readily that it is of far less importance than the other changes.

The appearance of secondary optic atrophy in a choked disc is of great prognostic importance and with experience it is possible to recognize optic atrophy while a choked disc is still present. If optic atrophy is well advanced, the vision may continue to fail even if the choked disc has been relieved by the removal of a tumor; a patient may even go on to blindness in such a case.

The question has been raised, can a patient who is blind as a result of a choked disc ever regain any vision? I have never seen a patient, who has been blind even a brief time as a result of a choked disc, regain his vision; but I have seen several patients, blind because of a primary optic atrophy due to a pituitary tumor, regain normal vision. This I confess is difficult to explain, but I have assumed in such cases that we were dealing with a physiological block of the nerve.

There are a number of conditions which resemble a choked disc so closely that they are difficult to tell apart, and at times indistinguishable. In malignant hypertension, polycythemia, and true optic neuritis due to an inflammatory process, the picture is very similar. Even albuminuric retinitis at times may very closely resemble a choked disc. At times it may be possible to tell these apart only by considering other aspects of the clinical picture. In this connection I should like to emphasize that there still are points about the mechanism of choked disc that are not fully understood. There is some evidence indicating that the same mechanism may be producing the eye ground changes in several of these conditions. If this should prove to be correct, there would no longer be any justification for applying different names to these various eye ground conditions.

V. Subjective Visual Disturbances. The final group of visual disturbances which I want to refer to are the subjective ones. These are in the nature of hallucinations and may be grouped under two general headings —the hallucinations of form and those of color. An irritative lesion of a cortical center gives rise to these subjective sensations. The visual phenomena are different, depending upon the portion of the cortex that is in-

volved. As a rule, irritation of the visual center in the occipital lobe gives rise to hallucinations of color. The patient sees these colors in a certain portion of the perimetric field. Thus, for example, if the lesion is located in the right occipital lobe, the patient will see these colors in the left half of each visual field, since the right occipital lobe controls the vision in the right half of each retina. These colors are often described by the patient as coming from one side. In a right occipital lobe lesion they would therefore appear from the left side.

In a certain number of lesions of the temporal lobe, patients may have visual hallucinations of form. They may see peculiar things or persons. Individuals may appear deformed, they may see strange people or animals. Many of these hallucinations are very similar to those described by patients in delirium tremens, and it may be that alcohol affects the temporal lobe particularly, producing such symptoms. At times these visual disturbances may be very complicated. I recall one patient, a very intelligent school teacher, who always saw an Elizabethan pageant pass before her. She saw all this so vividly that she was able to describe the costumes accurately. This type of visual hallucination is closely allied, if not a part of, the irritative lesions produced in the temporal lobe, which were first described by Hughlings Jackson, and called by him "dreamy states." In these attacks the patient not only may see peculiar things but often also may hear strange voices; with all this he has a sense of unreality, not knowing where he is, and often forgetting his own identity.

These two types of visual hallucinations may constitute the auras preceding a Jacksonian convulsion. Associated with these visual disturbances there may often be field defects, and such a combination—visual aura, Jacksonian convulsion, and field defect—constitutes ample evidence on which to localize a lesion in the temporal or occipital lobe.

In trying to determine the location of a brain tumor, numerous methods need to be employed, but I have attempted only to point out the great importance of ocular signs and the significant rôle they play in the diagnosis of brain tumor.

THYROID ACTIVITY IN CHRONIC ARTHRITIS *

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Opinions differ as to the relationship between thyroid activity, as determined by the basal metabolic rate, and variations in the arthritic syndrome.

The increased incidence of arthritis in women, particularly near the menopause, and the association of myxedema and hypothyroidism with chronic arthritis have suggested to many that a deficient thyroid secretion might be a contributing factor in the production of arthritis. Pemberton and Tompkins [1] studied the basal metabolism of 29 cases and found the basal metabolic rate (B. M. R.) within normal limits (between plus and minus 10) in 80 per cent, the remainder being below normal. Cecil, Barr and DuBois [2] studied four patients with chronic arthritis in a calorimeter and concluded that there was no disturbance of metabolism. Boothby and Sandiford [3, 4] found the B. M. R. between plus and minus 15 in 93 per cent of 69 patients with chronic arthritis. In 115 cases studied by Hench [5] the B. M. R. was normal in 80 per cent. Swaim [6, 7] reported a total of 312 cases. The B. M. R. was normal in 61 per cent, below normal in 25 per cent (below 0 in 63 per cent), and above normal in 14 per cent. He concluded that "abnormal metabolism with a tendency to a minus rate is characteristic of arthritis, especially in early years, having a tendency to return to normal as the duration of the disease lengthens." Hall and Monroe [8] reported that, in 214 cases of which 106 were rheumatoid and 108 osteoarthritis, the B. M. R. was normal in 48 per cent and below normal in 43 per cent. However, the B. M. R. was below 0 in 75 per cent of the cases. Hence it would appear from the latter reports that the B. M. R. falls within accepted normal limits in the majority of patients with chronic arthritis, although most of the rates are below 0.

Hall and Monroe [8] have discussed the literature on the relation of endocrine dysfunction to arthritis.

The present study was undertaken to determine particularly: (*a*) the frequency distribution of the B. M. R. in patients with chronic arthritis; (*b*) whether any particular range of B. M. R. is characteristic of any one type of arthritis; (*c*) the relation between the B. M. R. and disease activity, as indicated by the sedimentation rate and non-filament cell count; (*d*) the relation between the duration of the disease and the B. M. R.; and (*e*) the effect of the administration of thyroid extract upon the course of the disease.

A total of 684 B. M. R. determinations was made on 400 patients se-

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lected without discrimination on admission to the clinic. In those cases in which the results were checked, the lowest figure was considered correct.

The relationship between the B. M. R. and activity of the disease was studied by making serial tests during the course of treatment. The sedimentation rate and non-filament cell count were done simultaneously with the B. M. R. determination. Rates between plus and minus 10 were considered normal.

TABLE I

Distribution of Basal Metabolic Rates in 400 Patients with Chronic Arthritis

Type of arthritis	Sex	Number of cases	Basal metabolic rates							
			% +31 to +40	% +21 to +30	% +11 to +20	% 0 to +10	% 0 to −10	% −11 to −20	% −21 to −30	% −31 to −40
Rheumatoid	M.	48		2.1	8.3	16.7	29.2	37.5	6.2	
	F.	93	6.4	8.6	14.0	25.7	30.0	10.8	4.3	
Mixed	M.	32		6.0	3.1	6.0	59.5	21.9	3.1	
	F.	111	0.9	0.9	13.5	29.8	32.5	15.2	6.3	0.9
Osteo	M.	42		2.4	9.5	14.6	45.3	19.0	9.5	
	F.	74		5.4	8.1	33.8	28.7	17.6	2.7	2.7

FREQUENCY DISTRIBUTION OF BASAL METABOLIC RATES

Table 1 shows the distribution of B. M. R. in the different types of arthritis. The rates were normal in 59 per cent, below normal in 24.3 per cent (below 0 in 58 per cent), and above normal in 16.7 per cent of all cases, which agrees with the proportions found by Swaim.[6, 7] The distribution of B. M. R. was essentially similar in the different types of arthritis, except that there were more cases with B. M. R. above normal in the rheumatoid group.

In 141 patients with rheumatoid arthritis, the B. M. R. was above normal in 22.6 per cent, normal in 52.5 per cent, and below normal in 24.9 per cent.

In 143 patients with mixed arthritis, the B. M. R. was above normal in 13.2 per cent, normal in 63.8 per cent, and below normal in 23.0 per cent.

In 116 patients with osteo-arthritis, the B. M. R. was above normal in 12.0 per cent, normal in 63.0 per cent, and below normal in 25.0 per cent.

RELATION BETWEEN THE BASAL METABOLIC RATE AND ACTIVITY AND DURATION OF THE DISEASE

In table 2, the mean sedimentation rate (Westergren method), non-filament cell count, and duration of the disease in months are arranged ac-

TABLE II

Comparison of the Basal Metabolic Rate with the Sedimentation Rate, Non-Filament Cell Count and Duration of the Arthritic Disease

Findings compared	Type of arthritis	Basal metabolic rate									
		+31 to +40	+21 to +30	+11 to +20	0 to +10	0 to −10	−11 to −20	−21 to −30	−31 to −40	Mean +10 and above	Mean −10 and below
Number of tests	Rheumatoid	7	14	25	50	66	38	10			
	Mixed	1	4	26	50	75	34	8			
	Osteo		5	11	34	43	22	6	2		
Mean duration of disease in months	Rheumatoid	43	60	53	41	44	54	43		55.4	49.7
	Mixed	17	88	10	64	91	76	103		93.9	76.4
	Osteo		69	64	44	44	77	37	69	65.7	57.3
Mean sedimentation rate	Rheumatoid	30	35	34	25	28	23	17		33.8	19.9
	Mixed	38	10	22	19	24	19	15		23.0	16.7
	Osteo		7	9	19	23	21	10	14	14.4	11.2
Mean non-filament cell count	Rheumatoid	21	23	18	15	18	14	11		19.0	13.3
	Mixed	9	11	16	14	24	13	13		14.8	12.7
	Osteo		10	15	15	17	15	11	16	13.5	11.7

cording to the type of arthritis and the B. M. R. On the basis of 527 tests made on 341 patients, the following relationships were found. The sedimentation rate, non-filament cell count and duration of disease were higher in all groups with basal metabolic rates above normal. This was particularly true of patients with rheumatoid arthritis, the mean sedimentation rate being 33.8 mm. in the above normal group and 19.9 mm. in the below normal group and the mean non-filament cell count being 19.0 in the above normal group and 13.3 in the below normal group.

EFFECT OF THE ADMINISTRATION OF THYROID EXTRACT

Thyroid extract (Lilly) was administered to a number of patients with chronic arthritis, with the following results. Only 20 per cent of patients with markedly active rheumatoid arthritis showed improvement. Many patients could tolerate only small doses and, in some instances, it was necessary to discontinue it. In other patients there was increased resistance to intercurrent infection, the appetite improved and there was a sense of well-being. However, both the joint symptoms and the B. M. R. remained unaffected in these cases, even though the latter was below normal.

A number of patients who had shown marked hypersensitivity to vaccine tolerated larger doses and the arthritis improved when thyroid extract was also given. Patients who did not respond to thyroid extract alone improved when given vaccine also. Thus thyroid extract is a valuable adjunct in some cases, but it does not always bring about improvement when used alone.

About 41 per cent of patients with mixed and osteo-arthritis improved

following the administration of thyroid extract. This was particularly true in those cases involving the knee joints. Overweight women with large, swollen, tender, painful, stiff knees often had excellent results, particularly in reduction of swelling, increased motion and lessened pain. When the fingers were involved, marked improvement was often noted, particularly in early cases. Osteo-arthritis of the hip, spine or shoulders did not respond to the administration of thyroid extract, but good results frequently followed its use in inactive cases of the Marie Strumpell type of arthritis. The B. M. R. frequently became normal in patients with mixed and osteo-arthritis, but rheumatoid types were influenced only infrequently.

Discussion

The results obtained in the 400 cases reported in this paper confirm the reports of previous workers, that the basal metabolic rate is below 0 in 55 to 80 per cent of patients with chronic arthritis.

The smaller number of B. M. R. below normal in the present series of cases as compared with those reported by Hall and Monroe [8] may be explained, as they pointed out, by several factors. For example, ambulatory patients, such as those studied in the present series, have higher B. M. R. than hospital patients. Further, constant pain, causing insufficient rest and sleep, increased nervousness, etc., all tend to increase the B. M. R. This lends support to the contention of Hall and Monroe [8] that the calculated B. M. R. in these patients is always higher than the true rate. Assuming that the calculated rates were about 10 per cent too high, and adjusting the observed rates by this correction, 82 per cent of the patients in the present series will be found to have a B. M. R. below 0.

Poor nutrition of the joint has long been considered a causative factor in hypertrophic arthritis and, for that reason, this type of arthritis has been referred to as "degenerative" or "senile." The occurrence of several signs of hypothyroidism in patients with osteo-arthritis led Hall and Monroe [8] to believe that a lack of thyroid secretion was a factor in the etiology of these cases. Swaim [6] suggested that a low B. M. R. may precede arthritis. It is quite possible that a decreased secretion of thyroid hormone may affect the nutrition of the joints. Osteo-arthritis may also result from long-continued inadequate repair of traumatized joints. This theory is supported by the fact that joints, such as those of the hips, spine, knees and fingers, which are subject to considerable mechanical stress and strain are most frequently involved in hypertrophic arthritis. However, this theory may not apply to rheumatoid arthritis, in which case infection probably plays a prominent rôle and lowered metabolism is only one of a long chain of effects.

The B. M. R. is increased in the active stage of early rheumatoid arthritis, but is reduced when the disease becomes chronic, even though signs of active infection may still persist. As the disease becomes less active and ankylosis begins to develop, the B. M. R. tends to return to normal.

In the chronic stage, the brunt of the toxemia falls upon the liver, producing symptoms of intoxication of that organ in addition to those already affecting the thyroid. Usually there is also anemia, loss of weight, nervousness, emotional instability, rapid pulse, poor appetite, etc. In studies made in this clinic,[9] 73 per cent of such patients had liver dysfunction as judged by the Azorubin S appearance time. We[9] have confirmed Davis'[10] findings that the majority of these patients have lowered serum proteins and a reversal of the serum albumin-globulin ratio. The B. M. R. was below normal in 90 per cent of patients with abnormal Azorubin S appearance times and altered albumin-globulin ratios.

In the ankylosing stage the improved B. M. R. can be explained by lessened toxemia which permits the liver and thyroid to return to normal function. It is characterized by the disappearance of nervousness, irritability, poor appetite and depression. The color improves and the patient assumes a more cheerful attitude. This change is so noticeable that, when it does occur, it reminds one of the crisis in pneumonia. The rate of appearance of the three stages varies considerably with different patients. Sometimes the ankylosing stage is reached in a few months, while in other cases it requires several years.

The sequence of lowered B. M. R., abnormal Azorubin S appearance time, and alteration of the serum albumin-globulin ratio, although not always occurring in this order, appear to be additional progressive effects of the infection in rheumatoid arthritis and must be corrected to obtain best therapeutic results.

In rheumatoid arthritis it is difficult to influence a low B. M. R. On the other hand, in a large number of patients with mixed and osteo-arthritis, the B. M. R. can be increased with thyroid extract. Its value in these cases is as an adjunct to other forms of treatment and it should never be considered as an adequate remedy by itself. Successful thyroid medication is characterized by reduced nervousness, fatigue and depression, improved appetite and sleep, and by other signs of constitutional improvement.

Conclusions

1. The basal metabolic rate was within normal limits in 59 per cent, below normal in 24.3 per cent, and above normal in 16.7 per cent of 400 patients with chronic arthritis.

2. The number of cases showing basal metabolic rates below normal was essentially similar in the rheumatoid, the mixed arthritic and osteo-arthritic cases. However, in the rheumatoid group more cases showed rates above normal than in the other two groups.

3. In patients with mixed and rheumatoid arthritis, the basal metabolic rate varied with the activity of the disease.

4. The duration of the disease was greater in those patients with a basal metabolic rate above normal than in those with normal or sub-normal rates.

5. Small doses of thyroid extract, although not curative per se, frequently produced some improvement in joint symptoms and raised the general resistance.

6. Thyroid extract is more effective in the mixed form of arthritis and in osteo-arthritis than in rheumatoid arthritis.

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PLASMAPHERESIS EXPERIMENTS UPON THE INFLUENCE OF COLLOID OSMOTIC PRESSURE, WATER AND SALT IN EDEMA FORMATION*

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NUMEROUS investigators have produced edema by a reduction of the plasma proteins. The reduction of the plasma proteins by repeated bleedings is called plasmapheresis. Leiter [1, 2] and Barker and Kirk [3] were the first to carry on this work. Since that time numerous investigators, chiefly Shelburne and Egloff,[4] Lepore,[5] Darrow, Hopper and Carey,[6] Weech, Snelling and Goettsch,[7] Kylin [8] and ourselves [9, 10] have carried on these experiments. Our method of plasmapheresis has been essentially the following: Five to eight hundred cubic centimeters of normal blood were obtained from the right or left ventricle of a normal dog. This blood was citrated, centrifuged, the plasma thrown away and the cells, after having been washed several times with Ringer's solution, were suspended in Ringer's solution in an amount sufficient to bring them to the original volume. The dog whose proteins were to be lowered was then placed on the table, a right heart puncture was done, and 500 to 800 c.c. of blood were removed depending upon the size of the dog. The cells of the first dog suspended in the Ringer's solution were then injected into the jugular vein of the second dog. The blood removed from the second dog was then centrifuged and the cells washed and suspended in Ringer's solution up to the original volume for the purpose of future reinjection. Reinjection of red cells in plasmapheresis experiments is necessary in order that anoxemia be excluded as a factor in edema formation. This process was repeated several times a day, depending upon the type of experiment. The dogs were allowed to drink as much water as they desired during the course of the experiment and were given previously determined amounts of either saline or water by stomach tube at each bleeding. A record was kept of the weight of the dog, the amount of blood removed, the amount of fluid intake, the amount of fluid output, the plasma protein level, the osmotic pressure of the plasma colloids, and the amount of edema. When we first undertook plasmapheresis for the purpose of developing edema in dogs, we decided to give only water by mouth, using no saline. Both Leiter, and Barker and Kirk, gave large daily amounts of saline to their dogs during the time they were attempting to produce edema. We thought that such large amounts of salt would have some effect on the amount of edema produced because correspondingly large doses of salt given to

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a nephrotic patient would be sufficient to bring on massive edema. Therefore in our first experiments we gave the dogs only water. We carried on several experiments under these conditions and were disappointed to find that we could not produce a marked edema. Despite the fact that we reduced the blood proteins to levels far below those at which Leiter, and Barker and Kirk obtained edema and despite the fact that the osmotic pressure of the plasma colloids was far below that of the usual nephrotic patient with edema, only a tendency to edema was produced. Slight edema would be formed quite readily whenever some other factor such as the application of straps about the legs or injury to a vein through frequent puncture produced an increase in venous pressure. In one such experiment (table 1) which lasted over a period of 13 days, the dog was given 14,500 c.c. of water and put out 13,730 c.c. of urine. The colloid osmotic pressure was reduced to values of 5.6 to 6.9 mm. Hg.* At autopsy the dog showed practically no edema. Having failed to obtain any considerable amounts of edema by this method, we decided to repeat the experiment, using saline instead of water. In one such experiment (table 2) which lasted over a period of five days, the dog was given 7425 c.c. of saline and urinated only 3820 c.c. He developed marked ascites and anasarca. A comparison of the two tables shows that the colloid osmotic pressure was reduced to approximately the same level in both experiments. Yet in the experiment where saline was given instead of water, the dog developed massive edema.

These experiments, of course, lead us to certain definite conclusions: namely, that salt is necessary in the formation of edema and that without salt, even though the colloid osmotic pressure be reduced to very low levels, only little if any edema can result (unless other factors such as a rise in venous and capillary pressures develop at the same time). We then attempted to produce edema in a 24 hour period by repeated bleedings during the day. Table 3 gives the results of such an experiment. Five thousand six hundred cubic centimeters of blood were removed by repeated bleedings and replaced with red cells and Ringer's solution in a 24 hour period. The dog was given 4760 c.c. of fluid and put out 940 c.c. of urine. We also made an attempt to study the salt intake and output on this dog. It was found that he took in 30 gm. of salt during this period and put out 9.25 gm. in the urine. In other words, there was a retention of 5.5 grams of salt per liter of water. This dog had marked edema at death. There were 500 c.c. of ascitic fluid and the tissues of the neck and legs showed free fluid on section.

Having demonstrated that it was possible to produce edema by reduction of plasma proteins in a 24 hour experiment, we decided to attempt the following type of experiment (table 4). Instead of suspending the cells in Ringer's solution before reinjecting them, we suspended them in 6 per cent gum acacia solution. The experiment was carried out in exactly

* Normal for the dog is 18.6 mm. Hg.

TABLE I

Date	Wt. of dog, lb.	Blood removed c.c.	Fluid given c.c.	Urine output c.c.	Specific gravity	Albumin %	Globulin %	Fibrinogen %	Total Prot.	Osmotic pressure in mm. Hg	Edema
8/17/31	30	1000	900 H_2O	650	1.005	3.49	2.69	0.41	6.59		
8/18/31		1050	650 H_2O	1325	1.009	3.05	1.37	.29	4.71	17.9	
8/19/31		1075	1450 H_2O	1300	1.006	3.1	1.52	.40	5.02		
8/20/31		1050	1150 H_2O	750	1.007	2.27	1.04	.33	3.64		No edema
8/21/31		775	1450 H_2O	1210	1.007	1.97	.98	.26	3.21		Slight edema in legs below ropes.
8/22/31		1200	1700 H_2O	1725	1.010	2.08	1.28	.39	3.75		Slightly more edema below ropes.
8/23/31		500	1050 H_2O	1100	1.007	1.78	1.14	.46	3.38		Slight edema.
8/24/31		1000	1700 H_2O	1315		1.32	.99	.35	2.66		Slight edema.
8/25/31		800	450 H_2O Dog Vomiting	540	1.011	1.03	.88	.30	2.21	5.6	Little edema in hind legs
8/26/31		1000	800 H_2O	790	1.010	1.31	1.07	.40	2.78		Slight edema on body and legs
8/27/31		1000	1500 H_2O	1025	1.010	.93	.95	.22	2.10		Same
8/28/31		500	1700 H_2O	2000	1.009	1.34	.80	.34	2.48		Only small amounts of edema of legs and body
		Total	14500	13730							

Autopsy showed only slight edema on the legs and body. No ascites.

TABLE II

Date	Wt. of dog, lb.	Blood removed c.c.	Fluid given c.c.	Urine output c.c.	Specific gravity	Albumin %	Globulin %	Fibrinogen %	Total Prot. %	Osmotic pressure in mm. Hg	Edema
10/6/31	26.5	1500	1500 saline	1100	1.015	3.8	1.69	0.44	5.93	17.3	
10/7/31		1500	1650 saline	1500	1.020	2.0	1.05	.44	3.49		
10/8/31		1500	1425 saline	350	1.032	1.49	.70	.44	2.63		Slight edema.
10/9/31		1000	1550 saline	425	1.021	.69	.47	.23	1.39	5.8	Abdomen distended with ascites. Slight edema of the legs
10/10/31	28.0	1000	1400 saline	450	1.045	2.29	1.12	.46	3.87	9.0	Pitting edema on legs and abdomen
		Total	7425	3820							

Autopsy showed ascites and marked pitting edema on the legs and abdomen.

TABLE III

Date	Weight, lb.	Blood exchanged	Fluid given	Fluid recovered	Specific gravity of urine	NaCl given	NaCl recovered in urine	Edema	Plasma proteins
2–15–33 7:30 a.m.	27.5	1600 c.c.	200 c.c. Ringer's intravenously 500 c.c. saline orally			1.68 4.5			
2–15–33 1:30 p.m.	28.5	1500 c.c.	200 c.c. Ringer's intravenously 500 c.c. saline orally			1.68 4.5			
2–15–33 7:30 p.m.	30.	800 c.c.	200 c.c. Ringer's intravenously 500 c.c. saline orally	500 c.c.	1020	1.68 4.5	7.15 gm.		At 7:30 p.m. Total protein 1.72%
2–16–33 12:30 a.m.	32.	800 c.c.	200 c.c. Ringer's intravenously 500 c.c. saline orally 1000 c.c. H_2O taken	None		1.68 4.5			
2–16–33 8:30 a.m.	34.	800 c.c.	100 c.c. Ringer's intravenously 100 c.c. 30% acacia intravenously 500 c.c. saline orally	440 c.c.	1012	.84 4.5	2.12	Present	At 8:30 a.m. Total protein 2.56%
2–16–36 4:30 p.m. Dog died			250 c.c. H_2O						
		Totals	4760 c.c.	940 c.c.		Total 30.06 gm.	Total 9.27 gm.	Marked	

Dog had 500 c.c. of ascites at death. Tissues showed free fluid in neck and legs on cutting into them.
Autopsy also showed 150 c.c. of bloody pericardial fluid.

TABLE IV

In this experiment, plasmapheresis was carried on as follows: The blood was centrifuged, the plasma discarded and the cells were made up to the original volume with 6 per cent gum acacia in Ringer's solution.

Date	Weight	Blood exchanged	Fluid given c.c.	Fluid recovered c.c.	NaCl given	NaCl recovered in urine	Plasma proteins	Colloid osmotic pressure mm. Hg	Edema
2–23–33 9 a.m.	19.5	700 c.c.	200 c.c. Ringer's intravenously 400 c.c. saline orally		1.68 gm. 3.6 gm.		After bleeding 0.97%		None
2–23–33 2 p.m.	21.5	700 c.c.	200 c.c. Ringer's intravenously 400 c.c. saline orally		1.68 gm. 3.6 gm.		Before bleeding 2.1%		None
2–23–33 7 p.m.		700 c.c.	200 c.c. Ringer's intravenously 400 c.c. saline orally		1.68 gm. 3.6 gm.		Before bleeding 1.12%		None
2–24–33 1 a.m.	21.0	700 c.c.	200 c.c. Ringer's intravenously 770 c.c. H_2O orally	2100	1.68 gm. 3.6 gm.		Before bleeding 0.97%	15 mm. Hg	None
2–24–33	Dog died		120 c.c. H_2O	480		20.07			None at autopsy
		Totals	3290 c.c.	2590 c.c.	21.1 gm.	20.07 gm.			

9.3 gm. of gum acacia were recovered in the urine.
Autopsy showed no edema—no ascites—veins were markedly distended.

TABLE V

In this dog no plasmapheresis was performed, but he was given water and salt in the same amounts as were the dogs on which plasmapheresis was done.

Date	Weight	Blood exchanged	Fluid given c.c.	Fluid recovered c.c.	NaCl given	NaCl recovered in urine	Edema
3–20–33 10:30 a.m.	17.5	None	400 c.c. saline orally		3.6 gm.		None
3–20–33 1 p.m.	18.5	None	300 c.c. Ringer's intravenously 400 c.c. saline orally		2.52 gm. 3.6 gm.		None
3–20–33 5:30 p.m.		None	300 c.c. Ringer's intravenously 400 c.c. saline orally		2.52 gm. 3.6 gm.		None
3–20–33 Midnight		None	200 c.c. Ringer's intravenously 400 c.c. saline orally		1.68 gm. 3.6 gm.		None
3–21–33	16.5		Water intake 100 c.c.	2400			None
			Total fluid 2500 c.c.	Total output 2400 c.c.	Total NaCl 21.1 gm.	Total NaCl in urine 19.9 gm.	

At the end of the experiment, there was no demonstrable edema.

the same manner as the previous experiment except for the addition of gum acacia. The blood proteins were reduced to levels far lower than those necessary to produce edema in any of our other experiments. However, in this experiment the colloid osmotic pressure of the plasma was at nearly the normal level for dogs. Under these conditions the dog was given 21 gm. of salt and excreted 20 gm. of salt. At autopsy there was no edema, the tissues were dry, and there was no ascites. It then became necessary to ascertain how a normal dog without any plasmapheresis would handle the same amount of water and salt. Accordingly, the experiment shown in table 5 was undertaken. In 24 hours the dog was given 2500 c.c. of fluid, mostly saline and Ringer's, and put out 2400 c.c. of urine. He took in 21 gm. of salt and excreted 20 gm. of salt. No edema was formed.

These experiments prove conclusively that the maintenance of the colloid osmotic pressure at the normal level by some inert colloid (gum acacia) is

TABLE VI

Summary of Experiments on Plasmapheresis in the Production of Experimental Edema

Types of Experiments	Plasma proteins	Colloid osmotic pressure	Excess salt	Edema
Plasmapheresis Dog drinking only water	Reduced	Reduced	Absent	None
Plasmapheresis Dog drinking saline	Reduced	Reduced	Present	Marked
Plasmapheresis replacing plasma with 6% gum acacia Dog drinking saline	Reduced	Normal	Present	None
No plasmapheresis Dog drinking saline	Normal	Normal	Present	None

This table shows that two factors are necessary in the production of experimental edema, namely reduction of the colloid osmotic pressure and adequate salt intake.

sufficient to stop any tendency to edema formation. Even when the protein levels were reduced to values far below the level at which edema usually appears in such an experiment when no gum acacia is given, no edema developed. These experiments prove conclusively that the tendency to edema formation is a function of the colloid osmotic pressure of the plasma and would tend to show that one of the main functions of proteins in the plasma is the maintenance of a normal colloid osmotic pressure. Table 6 summarizes the experiments on plasmapheresis and shows the effect of various factors in edema formation.

CONCLUSIONS

1. Plasmapheresis experiments on a dog in which the colloid osmotic pressure of the plasma is reduced to levels equal to or below those which

cause edema in man will not lead to edema formation or salt retention as long as the dog is given only water and a very much restricted intake of salt.

2. The same experiment leads to marked edema formation and salt retention when the dog is given normal saline instead of water.

3. Twenty-four hour plasmapheresis experiments in which the proteins are reduced to a very low level within 24 hours result in marked edema within this short period of time if the dog is given saline to drink.

4. Dogs in which plasmapheresis has reduced the protein level below the usual edema-forming level but in which the colloid osmotic pressure of the plasma has been maintained by an indifferent colloid, gum acacia, develop no edema or salt retention.

5. Normal dogs given large amounts of saline by stomach tube retain no water or salt.

6. Retention of salt is due to filtration of protein-free plasma as edema. Normally functioning kidneys will not excrete salt if it is prerenally deviated as edema by ultrafiltration in the capillaries.

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THE DOCTOR HIMSELF AS A THERAPEUTIC AGENT *

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In recent years there has been increasing talk about the broader aspects of medical service. Medical men themselves have been anxiously considering not merely the building stones of medicine, but the plan of the entire medical structure. A great foundation has recently asked us for a free expression of opinion concerning American medicine. We are asked how well is medicine fulfilling its function to society, how can the benefits of medical science be best distributed, how shall medicine best be meshed with the economic structure? And these questions have led to further questioning as to the values that we have for distribution. We have considered not only the question of whether the conduits for conveyance of medical service are open, but also the purity of the sources of supply. From all this free and even voluble outpouring of opinion, it has come to light that despite there being many expressions of opinion that are merely slogan-mongering, expressions with more than a tinge of trade-unionism in them, there is also emergent much well-considered thought, the thought of informed and able men.

In all this discussion there has constantly echoed one recurring phrase, a phrase which it is my purpose to consider here, a phrase that has sometimes been thought to have grown so threadbare that it has been designated as merely a " smoke-screen " to conceal some unavowed purpose, the phrase, " Personal relations between doctor and patient."

Those who have most used this phrase have not been the most liberal thinkers. It has been employed rather by men who heretofore had been disposed to regard medicine as a tight, fast-set science, men accustomed to emphasize the science, rather than the art, of medicine, men who had previously looked askance on discussions of human relationship as the vaporings of undisciplined thought. But now, from an unexpected quarter of the horizon, succor appears. In their anxiety to withstand change in the economic relationships of medical practice, these same men speak urgently of dangers to the relationship between doctor and patient. This relationship, which has received so little consideration in our councils, which has rarely been discussed at our medical meetings, has now become a citadel of refuge, a chief bulwark against socialization.

A recognition of the importance of the relationships between doctor and patient, even though belated, is none the less good. This relationship is indeed an overwhelming handicap to any plan for standardizing and mechanizing medical care. There are many things in medical work that can be standardized, to which methods of shop efficiency can be applied. The ap-

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plication of medical science to the care of swine and cattle has been best accomplished by mass standardization. The methods of pathology, immunology, clinical research and diagnosis have been brilliantly illustrated in our dealing with the domestic animals. In my State of Texas far more money is spent by the State on its veterinary service than on its public health work for human creatures, some evidence that the State is conscious that mass action is efficient in dealing with veterinary problems.

What distinguishes veterinary medicine from human medicine is just this relationship between doctor and patient. It is a relationship that has a long history. In the early history of medicine, it comprised all that the doctor had to offer the patient. It is only very recently that medicine has had more to give. A survey of medical history acquaints us with many illustrious names. Step by step these men contributed to an understanding of anatomy, physiology and to the description of clinical syndromes, but if we except such courage and consolation as the physician might offer, they had very little to give by which the patient could profit. Historians sentimentalize the practical values of ancient medicine. One scans the pages of Hippocrates in vain for any treatments of specific value. The pages of medical history read like the log of an old-fashioned ocean voyage, in which it is noted that on such a day a whale spouted, on such a day a flying fish was sighted, or a bit of driftwood, but in which no mention is made of the huge prevailing fact that what was constantly seen day by day, almost to the exclusion of other sights, was the unending green waste of water. And this inevitable circumambient ocean is, by analogy, in medical history the "personal relationship between doctor and patient."

By this it is not meant to say that doctors didn't do things for their patients. They did a great deal. The need of human beings for action when in distress, some sort of action, without much question as to whether the act was wise or foolish, was met. Medicine, as the anthropologists tell us, was originally magic. Pharmacology is a late development. Medicines were prescribed that produced an overt effect,—vomiting, sweating, purging.

In a word, the medicines used were placebos, something to please the patient. The doctor, himself, by words of cheer and comfort sought to please the patient. His medicines were merely symbols to reinforce this purpose. Perhaps I may seem to be stretching the meaning of the word, placebo. It is ordinarily taken to mean a procedure undertaken to gratify the patient's desire for active intervention, but which is understood by the doctor to be inert and useless. For example, a bogus puncture. There is, however, a second sort of placebo, which seems to be no less a placebo, in the employment of which the patient's attitude is the same, but where the doctor's attitude differs in that though the procedure is valueless, the doctor esteems it to be valuable. For example, an ovarian tablet. As to the first type of placebo little need be said. It is a type of treatment not uncommonly used, effective at times yet not held in high esteem. The second sort of placebo the type which the doctor fancies to be an effective

medicament but which later investigation proves to have been all along inert, is the banner under which a large part of the past history of medicine may be enrolled. The herbs of the Indians, the pharmacopeias of the Orient, a large part of the contents of our older books on medicine are made up of these placebos in which doctors erroneously had faith. Their usefulness was in direct proportion to the faith that the doctor had and the faith that he was able to inspire in his patients. But related to this second group of placebos is a third group, a group in which the placebo used while it is believed in by the doctor, is no longer harmless but harmful, sometimes very dangerous. It would seem peculiarly contradictory to speak of the painful and dangerous placebo, yet men are so constituted that they feel the need in dire extremity of resorting to dread measures. Nervous patients, in particular, feel that a certain standing and sanction is bestowed on their maladies when violent therapeutic measures are used.

The great lesson, then, of medical history is that the placebo has always been the norm of medical practice, that it was only occasionally and at great intervals that anything really serviceable, such as the cure of scurvy by fresh fruits, was introduced into medical practice. By and large, the doctors were, as reported by that sane and shrewd observer, Montaigne, a danger to their patients. The medical historian is apt to mislead us when he speaks of the learned and skilful doctors of the past. While undoubtedly exceptional instances might be unearthed to show that these physicians accomplished something for the somatic good of their patients, in the large view we are forced to realize that their learning was a learning in how to deal with men. Their skill was a skill in dealing with the emotions of men. They themselves were the therapeutic agents by which cures were effected. Their therapeutic procedures, whether they were inert or whether they were dangerous, were placebos, symbols by which their patients' faith and their own was sustained.

The history of medicine is a history of the dynamic power of the relationship between doctor and patient. Through centuries when doctors were doing more harm than good this dynamic force has sustained the medical profession in the esteem of their clientele, it has inspired their fellow citizens with such faith in its values that they were willing to give economic support to the doctor. However little the doctor had to offer, it was to him that men turned in the distress of illness. When we observe the honor and emolument bestowed on the physician throughout the ages we are forced to exclaim, "Oh rare cogency of the relation between doctor and patient."

The scene has changed. With the name of Pasteur we associate an increasingly rapid acceleration in our emancipation from the sway of the placebo. The prestige of medicine has constantly mounted higher and higher and this prestige rests on a solid foundation. So rapid have been the acquisitions in bacteriology, immunology, in sanitation, so increasingly efficient have we become in hygiene, in dietetics, in surgery, in the executive distribution of the scientific plans through departments of health and organizations for nursing, so great has been the eagerness to acquire new knowledge

and to institute fresh researches, that we have been tempted to forget our origins, the long historical past of "personal relations between doctor and patient." Not that there are not enough reminders of it. The relation between nostrum-vendors and their patients, between chiropractor and patient, between quack of whatever stripe and patient should suffice to remind us of our past. The fact that States and legislatures have shown themselves so kindly disposed towards the charlatan and his placebos gives one to see how strongly entrenched in the popular mind is the precedence of the healer-patient relationship over the claims of somatic medicine. No one considers applying the principles of osteopathy to pigs and steers, because osteopathy is a human relationship, a "personal relation between doctor and patient." It is not through cults that exploit personal relationship but through our knowledge of bacteriology, immunology and dietetics as embodied in veterinary science that the legislature is expecting to see swine and cattle brought sound and healthy to the slaughter pen.

What is the something more, something different from the veterinary medicine that the patient expects when he goes to the doctor? It is certain that were he subjected to Socratic questioning no very clear answers could be had. The patient is aware of the doctor's prestige but he is unaware of what sort of foundation it rests on. Between what he expected as magic potion or compelling ritual from the doctor-priest and what he expects from scientific medicine there lies a bond of kinship. For many a patient the drug prescription is still heavily tinctured with magic; for him the doctor is a medicine man, a drug-giver, and it may be regarded as an ameliorating circumstance that when such a patient strays off after a drugless cult in addition to being in revolt against common sense, he is also in revolt against outworn superstition.

But what the patient most imperatively demands from the doctor is, as it always was, action. However the doctor may spar for time by delays of diagnostic study, these delays only whet the patient's appetite for decisive action. In a large and constantly growing number of instances the physician is able quite satisfactorily to render the service expected of him. When it is a question of diabetes or myxedema, amebiasis or syphilis, beriberi or macrocytic anemia, the physician sets about his work with resolute confidence. In the group of diseases for which nursing care is our chief resort, bronchial pneumonia, typhoid fever, and the rest, the line of procedure is scarcely less well-defined. In situations of utterly hopeless outcome the physician at least understands that consolation and the relief of suffering is his rôle.

But what of the patients who fall into none of these classes? What proportion are they of all those that seek treatment? Sydenham estimated that they comprised a sixth of all his patients. Charles Emerson, in his recent book, estimates them as half, and estimates further that half the symptomatology of the somatically ill is nervous. These patients are even more demanding than the somatically ill for action. As a class they are

little inclined to listen to sheer reasoned counsel, however adroitly it may be worded. They are usually disposed to question the diagnosis if told they have no somatic disease. The approval of these patients is essential to the doctor's success in practice. What can he do? What he very often does is to treat them with placebos, coupling the placebo with such suggestions for improved mental hygiene, and better ways of living as he can sandwich in. If reproached for degrading the pharmacopeia to the rôle of placebo, these men retort, "Well, after all, a man has to be practical."

Often enough, doctors of little critical discrimination come to believe in the placebo just as their faith is able to impart to the patient the faith that heals, and the faith seems to be justified by its fruits. Such men argue hotly for their placebos, since it is a well-known trait of character that ire is engendered by matters of faith, not by matters of demonstration; men fight for a belief, not for a statistical deduction. These are they that loudly affirm "thou shalt have no other placebos before mine," and pursue with bitterness the alien placebo-mongerers of another cult.

When thoughtfully considered, this situation is not one to be regarded with comfort. Medical men are not without misgivings about the spurious psychotherapy that they are under constant temptation to practice. Yet the path to development of a better psychotherapy is full of obstacles. The doctor's training in the laboratory and the ward has offered few opportunities for the development of any aptitude in dealing with the problems of personality. Doctors consider that their vocation is to deal with things that can be weighed and measured and that the reactions of the cerebral cortex and the autonomic nervous system are too intangible for them to deal with. As a distinguished member of this body, and contributor to this program recently wrote me:

"I suppose that I am particularly bitter about the people whom we may as well call neurotics, who, as you say, take up so much of an internist's time. They are the people who drove me out of practice. I never could see any sense in paying any attention to them because, as your word picture of them so graphically shows, they have neither sense, nor gratitude, nor any idea of coöperation, nor any qualities that might endear them to man, woman or child.

"I cannot understand why those of us who have trained ourselves to take care of people who have organic disease can't be allowed to take care of organic disease. Why won't these people take our word for it that there is nothing the matter with them and let it go at that? I suppose I have as many somatic sensations as anybody on earth but I explain them to myself in a physiological way. Why can't an intelligent neurotic take the same sort of advice that I give myself? There seems to be no way of handling them except that sort of semi-quackery that some highly respectable members of our fraternity are able to get away with so successfully."

Here is a credo. There is a confession of faith. It has led a highly successful internist to give up his practice so he says, and seek other employ-

ment. It is as though one said "I don't like feces," and refused to treat dysentery or cholera. The brain and nervous system are organs of the body, their functioning is observed in behavior and feeling. Now, when it has become a pride of medical research that we study function, when studies of the function of the heart, the kidneys, the liver, are constantly multiplied, why refuse to consider the functions of the master tissues,—the brain and vegetative nervous system? Wouldn't it be about like refusing to consider disorders of the circulation though admitting a willingness to treat another system of the body?

And yet the above statement is one of the most logical statements that could be made. It is as logical as the rack and the faggot for the heretic. What could be more logical—when eternal torture in hell awaits the heretic —how humane to torture him now in order to spare him endless torture. The flaw in the logic is that there is no hell of eternal torture; the flaw in the logic of my correspondent is that behavior and feeling do not subsist in some separate ghostly realm but form a part of the organic activities of man. The postulate that underlies my correspondent's viewpoint is physiologically untenable.

And another thing—a rather base practical point to which I would like to invite you—is that my correspondent's view won't pay out. Not to refer to the fact that it has driven him from the practice of medicine (he is spoofing about that), a much worse thing is it will tend to drive patients away and drive many doctors to penury. In Germany this viewpoint has long existed. It was expressed by the Chancellor of Washington University today when he said, "The doctor had better stick to his last." The result of this credo in Germany has been that the offices of doctors are empty while those of naturopaths overflow, that quacks abound as nowhere else; that finally the Hitler Government has set up the quack as the State Medicine. The Führer in medicine is a Naturopath.

An even greater obstacle, however, lies in the patient himself. The patient's philosophy is usually the traditional one that the mind and body are quite distinct affairs, that he has come to see the doctor about his body, and that if the doctor begins to talk about psychic matters he is being cheated. There was a certain admirable unity in primitive days when the doctor-priest offered the magic potion to exorcise the demon of sickness. That unity has been lost. We now face a hopeless dichotomy. It will be an uphill road to try to explain to the patient the unity of the organism, that mind is an aspect under which the integrated body is to be regarded, that the soul represents the interplay between the organism and its external and internal environment. Any such talk the patient would regard as an evasion, as making light of his trouble, and the physician who expounds such views may find that his patient will seek another who is more in accord with his own viewpoint, and, as he will doubtless believe, possessed of a keener apprehension of the diagnostic problem.

But it is time to turn from the question of difficulties and consider

the search for a possible solution to this question of how to deal with the 75 per cent of nervous symptoms which present themselves in our patients, to consider dealing with them in some more thorough-going way than through the employment of tonics and sedatives, to seek whether there may not be something more admirable than the resort to placebos. In the first place it may be asked, can nervous symptoms be studied and dealt with by the methods of the exact sciences.

I have recently read a little book, " Einfluss der Gemütsbewegungen auf den Körper." In this account of the influence of emotional disturbances on the body, I find some 16 pages of bibliography devoted chiefly to a record of experiments, most of which attempt to weigh and measure those things that we are wont to call intangible. There are innumerable experiments recording the effect of emotion, not only on heart rate and blood pressure but on the size of the heart, not only on the titer of acidity of the gastric juice and on gastric motility but on the position of the stomach, not only on the frequency and amount of urinary output but on the chemical composition of the urine; experiments that indicate the effect of emotion on blood chemistry, on electrical reactions in the skin. Much of this subject matter was finely developed in Dr. Cannon's oration last year. These studies go far to show that what we have called intangible is really tangible. Emotional life does, it is true, admit of exact scientific study. From a consideration of these experiments we will indeed get many fruitful conceptions of great help in practical daily work. Physiological laboratories, however, deal as a rule with brief and elemental emotions. They have not yet arrived at the point where they can take account of these neuro-muscular dispositions that are concerned in hope and courage, in depression and loss of confidence, in the long rankling of envy or the serenity of peaceful acquiescence. Suggestive as are these studies, they do not put into our hands diagnostic instruments for the study of our nervous patients. Nor do they tell us in any unequivocal way what we must do for them.

Another solution that has in recent times been much emphasized is that the practitioner of medicine should acquire the psychiatric viewpoint. There must be a closer liaison between psychiatry and medicine. There can be no doubt that internal medicine not infrequently is biased toward an explanation of symptoms as necessarily due to structural and chemical change when the true explanation lies in a disturbance of the emotional life. Nothing would seem more logical than that the psychiatrist, through his familiarity with the gross disturbances of reaction and behavior, should bring us help in dealing with milder disturbances. As the late Dr. Salmon pointed out, we cannot refuse to the study of the neuroses our active concern for the very good reason that we have accepted from the state the responsibility for the care and direction of the insane. If we accept the responsibility for the care of advanced sickness of the soul, we must all the more be attentive to an incipient sickness.

There can be no doubt that there does exist a chasm between psychiatry

and medicine. A circumstance that tends to widen the chasm is the profound reluctance of the nervous patient to be placed in the category of psychiatric patients. He insists, "I am not crazy," and resents even the suggestion that he may have symptoms that are not of somatic origin. It might be an excellent thing if all nervous patients could be cared for by skilled psychiatrists, but in many instances the very crux of the difficulty is that the patient does not consider himself a nervous patient. The battle in many cases would be nearly won if the patient could be induced to place himself in the hands of a psychiatrist, but actually the heat of the battle is over before the malady encounters its proper antagonist.

It is indeed true that the psychiatrists have contributed much to our understanding of the nervous patient, but the practitioner is likely to feel that the psychiatrist he knows is chiefly concerned with the problems of custodial care and has small opportunity to become conversant with such organ neuroses, such emotional problems as are daily encountered in practice. He scarcely understands that by the psychiatric outlook is meant a consideration of the broad issues of the dynamics of personality.

If the practicing physician turns to the school psychologists for aid, his findings may prove to be even more barren. Non-medical psychologists are at a considerable disadvantage in that they do not give sufficient weight to the problems of sleep and diet, the systole and diastole of effort and repose.

One cannot advance against the disorders in the emotional sphere by mere reasoning. By the emotional sphere is meant not merely fear, rage and sex-love, but the whole inner reaction-mechanism, the reactions of single organs, of functional systems, the reactions of mood, of desire, of the inclinations and vital drives of the integrated organism. It is these great vital tendencies that the psychobiologist conceives as furnishing the motive power. Their chief seat is the thalamus, the basal ganglia; their expression is through the autonomic nervous system. The intellect, the cortex is their servant; its mission to find means for their satisfaction. If the mind is the steering wheel, the emotional life is the motor, or, a better analogy, the vital tendencies dictate the direction and the goal while the mind finds the path that leads thither. It is well to seek new analogies to reinforce the truth that reason is servant, that vital tendencies as expressed in the emotional life are master.

As the patient faces the doctor he believes in certain things about himself which the doctor doesn't believe. The patient has faith in his malady which the doctor doesn't share. Faith is belief. It is a belief in which the thalamus has a stronger share than the cortex. The doctor's reasonable hope for cure rests on making such environmental changes as will alter the emotional status of his patient. The environmental factor of most moment is likely to be the physician himself. He will prevail if his faith is stronger than the patient's faith. Icy reasoning will not suffice. A strong enough faith, even in his placebos, may be enough, but as knowledge advances faith

in placebos declines. The faith needs a firm foundation. How shall such a foundation be laid?

A great deal is said about changes to be made in the patient's outlook and viewpoint. Not much about what the emotional attitude of the doctor shall be. Faith is an emotional attitude of warm confidence toward a situation. Freud, in discussing the "personal relationship of patient to doctor" asserts that for success in the relationship the patient must love the doctor, the so-called transference. This contribution to scientific exposition of the doctor-patient relationship is nothing to startle us. He doesn't say that the doctor must love the patient. Yet the doctor's attitude toward the patient is perhaps more fundamental than the patient's attitude toward the doctor. John Dewey, in his book, "A Common Faith," has shown that the faith to which all wise men, of whatever race or creed, may subscribe is a humanistic faith, and may be expressed as a sublimation and reinforcement of those human relationships that are cherished by every man. He must be a father filled with wise benevolence, a brother with consciousness that he shares in embryo all the weaknesses and frailties of the patient, a friend that knows the art of showing himself friendly.

Every man knows that emotional attitudes are more readily communicated than ideas. A dog or a child can understand an emotional attitude. The simplest souls can grasp the thalamic component of belief. The subtlest mind also yields to the persuasive drive of emotion, to the affective situation in which he finds himself. The dweller in the Orient unconsciously acquires enough of the spirit of acquiescence and inner calm to gain the low arterial tension of Oriental neighbors. The faith that heals, heals not through argument but by contagion. But to heal, faith must have substance. A speculative balance of probability is not enough. The faith that heals must have deep roots in the personality of the healer. A recent best seller in the realm of popular psychology, "The Return to Religion," written by a well-known psychologist, suggests as a cure for the feebleness of the doctor in the doctor-patient relationship that he return to the rites and formulas of the church. It is true that these express in fit and beautiful words many truths that seem to fade and perish when put into the clumsy terms of science.

But this suggestion won't help us. The faith about which reservations are kept has no living force. The faith that will avail the doctor must be grounded in his own psychobiologic conceptions. One of the most hopeful moves in medical education is teaching to first-year students the elements of psychobiology. A system of belief is implanted best in the young. It would be my suggestion that psychobiology be taught in the premedical years, that the doctor-patient relationship be the beginning of medical study. A deep insight into this fundamental philosophy is a chief concern of the internist.

I know no short definition of the word "internist," but I conceive of him that he is a type of general practitioner who, having delegated to workers in special fields a large number of his cares, has a special opportunity to gain

a vantage-point from which he can get a larger survey of the field of medicine. From this vantage-point he can see what problems press most instantly for solution. He it is who most correctly can select the point where therapeutic emphasis should fall, can judicially assay the worth of the rival claimants for priority in dealing with the sick man's problem.

To him then we would best address the question, " How can the 'personal relationship between doctor and patient' be made more fruitful for good? How can the doctor himself, as a therapeutic agent, be refined and polished to make of him a more potent agent?

" What shall be the foundation of his faith? Is he to employ the placebos that he scorns when employed by the uncultured, or is he to find a way to educate his public to demand something different, something far better of him? " I leave this discussion in the form of a question, but a very pertinent and pressing question. A right answer will lead to the physician's occupying a position of even greater dignity in the social order than the high place he now holds.

AN ARTICLE CONTRIBUTED TO AN ANNIVERSARY VOLUME IN HONOR OF DOCTOR JOSEPH HERSEY PRATT

ABSCESS OF MEDIASTINUM FOLLOWING ACUTE TONSILLITIS *

By CHESTER S. KEEFER, M.D., F.A.C.P., *Boston, Massachusetts*

AN abscess of the mediastinum is a rare complication of hemolytic streptococcal infection of the throat. Recently such a case was observed and, following surgical treatment, the patient recovered completely. A summary of the case follows:

CASE REPORT

Following an acute tonsillitis and pharyngitis, a man develops painful and difficult swallowing, pain between the shoulder blades, fever, and leukocytosis. Examination showed signs of a mass in the posterior mediastinum. Abscess containing hemolytic streptococci drained. Recovery.

A man, 46 years of age, was admitted to the Boston City Hospital on account of fever and sore throat. Five weeks previously he had an attack of coryza and tonsillitis but it was not severe enough to confine him to bed. He continued with his daily work for two weeks, when he was forced to remain at home on account of chills, fever, and difficult and painful swallowing. This was accompanied by attacks of coughing which were productive of mucopurulent sputum. During the third week of his illness the chills and fever continued and the pain and difficulty in swallowing increased. In addition, he had some pain and discomfort about the base of the neck which radiated into the occiput during swallowing. The temperature gradually became lower and he felt somewhat improved insofar as his sore throat was concerned, but the dysphagia continued.

The physical examination showed a man who was acutely ill and pale. He had very few complaints but it was difficult for him to swallow liquids or solid foods. The temperature was 101.5° F. The throat was red and the pharynx seemed edematous and swollen. Palpation of the pharynx failed to reveal any localized mass although the mucous membrane was swollen. The lymph nodes of the neck were not enlarged, and the thyroid was not palpable. The trachea was in the midline and it could be moved lateralward without discomfort; it moved up and down on swallowing but this caused some discomfort. There was no swelling of the neck and no areas of tenderness on deep pressure. The movements of the cervical spine did not seem limited in extent. The examination of the chest failed to show any abnormal areas of prominence and the superficial veins of the chest wall and the jugular veins were not swollen. There was no retromanubrial dullness, no displacement of the heart or mediastinum laterally. The lungs were clear throughout. The heart was in normal position and the sounds were clear. Over the upper dorsal spine there was dullness extending from the first to the fourth dorsal spine, and over this area the whispered voice and breath sounds were distinct and bronchial in character, but aside from these abnormalities there was nothing distinctly abnormal to be made out on physical examination of the chest.

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From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital and the Department of Medicine, Harvard Medical School, Boston.

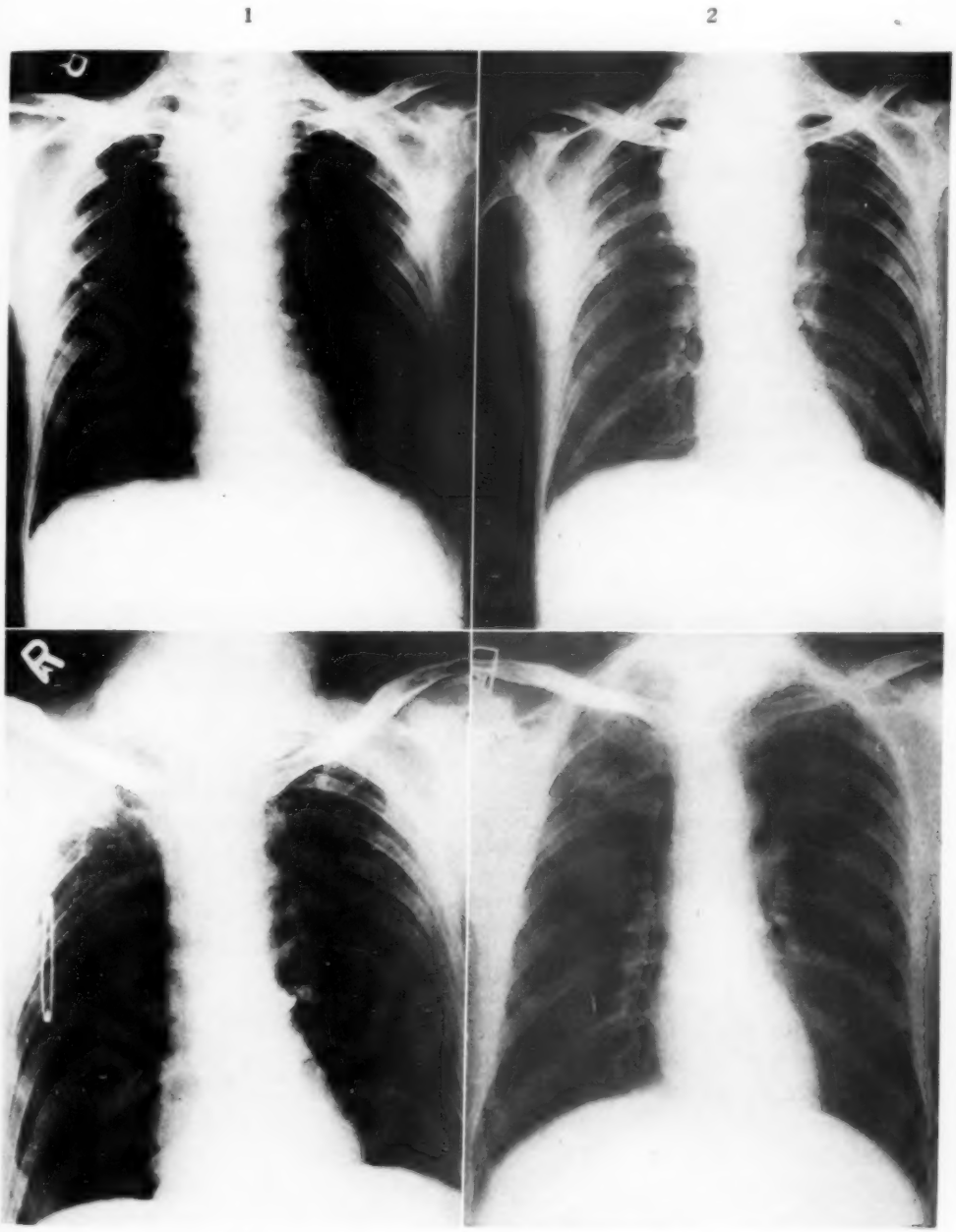

FIG. 1. Roentgen-rays of chest in patient with abscess of mediastinum. (1) Roentgen-ray on first day of admission. (2) Roentgen-ray on fourth day of hospital visit—note the enlarging mediastinal shadow. (3) Roentgen-ray of chest 4 days after operation. (4) Roentgen-ray of chest 2 months after operation.

The abdomen was soft and no organs were palpable. The extremities, genitalia, and reflexes were normal.

Laboratory examinations showed 3,860,000 red blood cells per cubic millimeter and hemoglobin of 74 per cent (Sahli). The total white blood cell count was 25,000 per cubic millimeter with 85 per cent polymorphonuclear cells. The urine was clear and normal.

The roentgen-ray examination showed the heart in normal position, the lung fields clear. In the superior mediastinum there was a bilateral rounded shadow with concave borders, slightly more prominent on the right side than the left. It was distinctly supra-aortic, and it had not displaced the trachea laterally nor the aortic arch downward (figure 1).

Fluoroscopic examination showed that this shadow was retro-esophageal and in the posterior mediastinum. The esophagus was displaced anteriorly and slightly to the left. As the barium entered the esophagus, it paused momentarily at this area before passing downward.

In summary, then, a man had an acute tonsillitis and pharyngitis which was followed by difficult and painful swallowing, fever, and leukocytosis. Examination of the chest showed decreased resonance and increased whispered voice sounds over the upper dorsal spine, a bilateral rounded shadow in the superior mediastinum by roentgen-ray, and anterior displacement of the esophagus by fluoroscopy. From the clinical course of the illness, together with the above findings it seemed highly likely that the process was an abscess in the posterior mediastinum. This clinical diagnosis was supported by surgical operation.

Course of Illness. The course of the temperature is shown in figure 3. On the seventh day of his hospital admission Dr. I. J. Walker operated by entering the posterior mediastinum, resecting a portion of the second, third, and fourth ribs close to their articulation with the spine, and opened an abscess containing 300 c.c. of thin purulent material. The pleura was not entered and a drain was inserted. Following the operation there was an increase in the temperature for several days, but it gradually subsided and returned to a normal level within 14 days. The pus from the abscess contained a pure culture of hemolytic streptococci and the drainage was profuse for several weeks. Due to the anemia, he received two blood transfusions and improved considerably. After several months the cavity gradually diminished so that very little drainage was evident. He gained weight and felt greatly improved. When he was seen two months after the operation, he appeared well, had returned to work, and there was only a small draining sinus in the back.

Comment

The subject of abscess of the mediastinum has been discussed most thoroughly in the classical monograph of Hare[1] on mediastinal diseases. More recent essays on the subject are those of Neuhof,[2] Fischer,[3] Lerche,[4, 5] Lambert and Berry,[6] Heuer,[7] Graham, Singer and Ballon,[8] Farnum,[9] and Malnekoff.[10]

In the present case, it seems likely that the infection of the posterior mediastinum resulted from an extension of the infective process in the pharynx to the retrovisceral space. The anatomical relations are illustrated in figure 2, which is reproduced from Lerche's[4] paper. It is seen that the retrovisceral space extends directly from the pharynx at the base of the skull to the posterior mediastinum. The other possibility, of course, is that the abscess arose from suppurating lymph nodes in the posterior mediastinum.

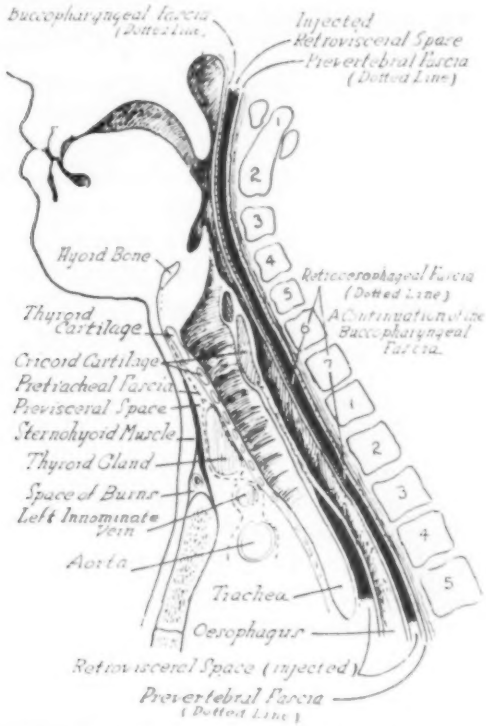

FIG. 2. Diagram showing injected retrovisceral space. (Reproduced by permission of Dr. William Lerche, Arch. Surg., 1924, viii, 247.)

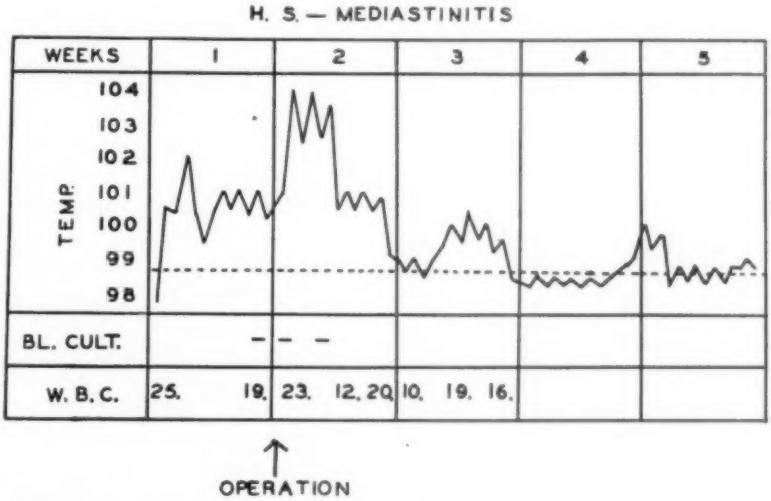

FIG. 3. Temperature chart of patient with hemolytic streptococcal abscess of mediastinum. White blood cell count is recorded in thousands.

This type of infection has been studied extensively by Lerche [5] who emphasizes the importance of mediastinal lymph node infections in the causation of mediastinitis. It is analogous to the retropharyngeal lymph node infections with abscess formation in children, the main difference being in the location of the infection.

In general, acute mediastinitis is uncommon but, inasmuch as a small number of these cases are of such a nature that they can be treated surgically, it is of importance that they be recognized. For purposes of discussion, it is convenient to divide these cases into two main groups: (1) the diffuse phlegmonous variety and (2) localized abscesses of the mediastinum. Inasmuch as the diffuse phlegmonous variety may be only a part of a more widespread infection and therefore not amenable to treatment it can be dismissed from the present discussion.

Localized abscesses in the mediastinum can be divided, according to the situation of the suppurative process, into abscesses in the anterior or posterior mediastinum. This division is of considerable significance insofar as treatment is concerned.

Abscess of the Anterior Mediastinum. An abscess in the anterior mediastinum results from: (1) an extension of an infection from the neck, such as erysipelas, or infection following surgical operations, (2) an osteomyelitis of the sternum, (3) suppuration of lymph nodes, (4) an extension of an infection from the lung to the mediastinum. An abscess in this location tends to extend to the exterior and may present in the suprasternal notch or at the anterior border of the sternomastoid muscle. It may gravitate downward and cause a painful, tender area in the region of the xiphoid. Rarely such abscesses may point beneath the sternoclavicular region or perforate into the interspaces in the parasternal line.

Abscess of the Posterior Mediastinum. An abscess in the posterior mediastinum results from an extension of an infection from the retropharyngeal space or from the esophagus. Other causes are extension of an infection from the spine, abdomen, lung, or pleural cavity. These abscesses show only a slight tendency to approach the surface and they commonly extend upwards or downwards in the mediastinum. They may rupture into the pleural cavity, the trachea, bronchi, esophagus, or pericardium. Indeed, when they are unrecognized or neglected they may even point in the posterior triangle of the neck or extend to the retroperitoneal space and appear in the groin.

Symptoms and Signs Referable to the Chest or Extension of the Infection to a Neighboring Organ. In the main, symptoms arising from pressure of various anatomical structures of the mediastinum are less conspicuous with an abscess than with a neoplasm, and at the onset the symptoms of infection predominate; it is only later that the symptoms and signs of compression occur.

Pain beneath the sternum and radiating into the back, or pain between

the shoulder blades or referred along the intercostal nerves on one side are common features.

The irritative phenomena consist of cough, dyspnea, painful and/or difficult swallowing, and painful movement of the trachea, or paroxysmal hypertension. Dysphagia is present when the process is situated in the posterior mediastinum and wheezing respiration occurs when there is compression of the trachea or bronchi; on rare occasions the bronchi may be compressed to such an extent that atelectasis occurs.

On occasions, the development of a mediastinal abscess is so insidious that it may be obscured by the symptoms and signs resulting from the extension of the process to a neighboring organ. The various paths of extension of an infection from the neck or mediastinum have been studied extensively by Lambert and Berry,[6] Furstenberg and Yglesias [11] and Coller and Yglesias.[12] It is well to be familiar with the various possibilities, since foci of infection may appear in various areas and have their origin in the mediastinum. Thus, one may find extrapleural abscesses, empyema, abscesses in the neck, or perforation of the trachea, bronchus, esophagus, or lung. More rarely the infection extends to the pericardium, the peritoneum, or the retroperitoneum. Infections in these areas, then, should call one's attention to the mediastinum as a possible focus of infection.

Roentgen-Ray Examination of the Chest. The roentgen-ray of the chest will show unilateral or bilateral triangular shadows with the apex pointing caudad and superimposed on the heart shadow, or there are rounded or triangular shadows in the superior mediastinum. There may be an associated empyema or extra-pleural abscess which obscures the lung fields. In the case of abscesses in the posterior mediastinum, the esophagus is often displaced anteriorly and to either side of the midline. All of these signs should be looked for and, when they are present, the diagnosis of mediastinal abscess should be entertained. The examination of the patient under the fluoroscope should include both an anterior-posterior view as well as a lateral one. The roentgen-ray diagnosis has been discussed recently by Kornblum and Osborn.[13]

Diagnosis of Mediastinal Abscess. The diagnosis of an abscess of the mediastinum depends upon the following features:

1. A history or the presence of a condition which is capable of causing a mediastinal infection.
2. The constitutional symptoms and signs of an infection.
3. The localizing symptoms and physical signs in the mediastinum due to involvement of various anatomical structures.
4. Signs resulting from an extension of the process to neighboring organs.
5. Characteristic roentgen-ray findings in the chest.
6. Finding an abscess on exploration.

When the above features are present one is justified in making a diagnosis of acute mediastinal abscess.

Treatment. The diagnosis should be made as early as possible, inasmuch as the only possibility of recovery is surgical drainage of the abscess. There are, of course, the exceptions in which the abscess is drained by rupture into a bronchus [9] or the esophagus, or by aspiration.[10] These instances occasionally occur when the abscess is overlooked and, while recovery may follow such a rupture, it is more common for death to follow such an accident.

In the present case, the posterior approach was used with success. Other methods which are recommended are drainage of the abscess through an incision in the neck with a drainage tube inserted into the mediastinum from this point.

Summary and Conclusions

A case of abscess of the posterior mediastinum following tonsillitis due to hemolytic streptococcus infection is recorded. Complete recovery followed surgical drainage of the posterior mediastinum. The clinical features and the course of these abscesses are summarized.

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AN ARTICLE CONTRIBUTED TO AN ANNIVERSARY VOLUME IN HONOR OF DOCTOR JOSEPH HERSEY PRATT

CORONARY ARTERY DISEASE; A HISTORICAL SKETCH *

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INTEREST in any subject is usually accentuated by some study of its early history, and in connection with some of the now well understood diseases a fascinating story may be written.

Medical students of 20 years ago seldom, if ever, heard of the clinical diagnosis of coronary thrombosis. Angina pectoris on the other hand was frequently discussed; that diagnosis, when made, carried with it in the minds of most, the sentence of a short life, terminating in sudden death. Now-a-days coronary thrombosis is up for daily discussion in a routine hospital visit; a fairly good guess can be made as to what artery is out of function and to the surprise of many, more than half of the patients go on to a satisfactory recovery.

This short sketch will make no attempt to cover clinical or pathological detail but will deal with incidents and men and their places in the development of our knowledge of coronary artery disease. The story, in this instance, as everyone knows, really began with William Heberden, whose first observations were made public in 1768. These were reported at a meeting of the Royal College of Physicians in London. Even at the risk of tedious repetition, some of his description will be quoted. He had just been referring to the various types of chest pain, vague, inconsequential and otherwise. Then he said:

> But there is a disorder of the breast marked with strong and peculiar symptoms . . . and not extremely rare, which deserves to be mentioned more at length. The seat of it, and sense of strangling, and anxiety with which it is attended, may make it not improperly be called angina pectoris.
>
> They who are afflicted with it, are seized while they are walking (more especially if it be up hill, and soon after eating), with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life, if it were to increase or continue; but the moment they stand still, all this uneasiness vanishes.
>
> In all other respects, the patients are, at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different. The pain is sometimes situated in the upper part, sometimes in the middle, sometimes at the bottom of the *os sterni*, and often more inclined to the left than to the right side. It likewise very frequently extends from the breast to the middle of the left arm. The pulse is, at least sometimes, not disturbed by this pain, as I have had opportunities of observing by feeling the pulse during the paroxysm. Males are most liable to that disease, especially such as have passed their fiftieth year.
>
> After it has continued a year or more, it will not cease so instantaneously upon standing still; and it will come on not only when the persons are walking, but when

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they are lying down, especially if they lie on their left side, and oblige them to rise up out of their beds. In some inveterate cases it has been brought on by the motion of a horse, or a carriage, and even by swallowing, coughing, going to stool or speaking, or any disturbance of mind. . . . In one or two persons, the pain has lasted some hours, or even days; but this has happened when the complaint has been of long standing, and thoroughly rooted in the constitution: once only the very first attack continued the whole night.

I have seen nearly a hundred people under this disorder, of which number there have been three women, and one boy 12 years old. All the rest were men near, or past the fiftieth year of their age.

The termination of the angina pectoris is remarkable. For if no accident intervene, but the disease go on to its height, the patients all suddenly fall down, and perish almost immediately.

One hundred and forty-three years later, before the same society, Sir William Osler, in his second Lumleian lecture said "Had Heberden listened to my first lecture he could have remarked very justly: 'Well! they have not got much ahead since my day.' In descriptive symptomatology we have not, and among 100 cases of angina pectoris there is no reason why Heberden should not have met all the important anomalies and complications. He had the good sense not to say much about the cause of the disease, and the good fortune to get very close to the truth in what he did say."

Contemporary with Heberden, were John Hunter, Edward Jenner and John Fothergill. These four were all in more or less intimate association with each other. It is of interest to note the possibility of discussion and conference between these men who, during the life of Heberden, cleared up this subject in such a way that little was added to it for another hundred years.

Hunter, himself, as everyone knows, was a victim of the disease. He was the greatest of the group, being ranked by Garrison along with Paré and Lister as one of the three greatest surgeons of all times. He was 45 years of age at the time of his first attack of angina, with which he was to be tormented for 20 years. Knowing his ailment he said, "My life is in the hands of any rascal who chooses to annoy and tease me." In a fit of anger at a meeting of the governors at St. George's Hospital, he had an attack, left the room and fell dead.

Heberden, a typical practitioner of that time, was 58 years old at the time of his first publication. He was a Cambridge graduate and an outstanding Greek and Hebrew scholar. His commentaries were written in Latin and were published in 1802, a year after his death. Of this it has been said —"The little book is one of the shining monuments of medical scholarship." Heberden died at the age of 91.

Fothergill, but two years younger than Heberden, was a Quaker, a successful and wealthy London practitioner, a friend of William Hunter. He was also a friend of Franklin and of the American colonies and in some measure aided in the founding of the Pennsylvania Hospital. He, in 1776, reported a fatal case which came to autopsy. The autopsy was performed

by Hunter whose description was rather meagre, the findings being in the main, negative, except as expressed in the last sentence as follows: "The two coronary arteries from their origin to many of their ramifications upon the heart were become one piece of bone."

Jenner, the youngest of the four, was a favorite pupil of Hunter's and a close friend for many years. He was in practice at Berkeley in Gloucestershire and at this time was 27 years of age. Hunter, in the year 1776, the same in which he did the autopsy for Fothergill, had his second attack of angina. While he was convalescing at Bath he consulted Jenner about his ailment, who, in turn wrote to Heberden giving his diagnosis. The letter in part was as follows:

"When you are acquainted with my motives I presume you will pardon the liberty I take in addressing you. I am prompted to it from a knowledge of the mutual regard that subsists between you and my worthy friend, Mr. Hunter. When I had the pleasure of seeing him at Bath last autumn I thought he was affected with many symptoms of the angina pectoris. . . . Though in the course of my practice I have seen many fall victims to this dreadful disease, yet I have only had two opportunities of an examination after death." He then describes the condition of the coronary arteries which he had noted at autopsy, adding, "As the heart, I believe, in every subject that has died of the angina pectoris, has been found extremely loaded with fat, and as these vessels lie quite concealed in that substance, is it possible this appearance may have been overlooked? The importance of the coronaries, and how much the heart must suffer from their not being able duly to perform their functions (we cannot be surprised at the painful spasms), is a subject I need not enlarge upon, therefore shall just remark that it is possible that all the symptoms may arise from this one circumstance.

"As I frequently write to Mr. Hunter I have been some time in hesitation respecting the propriety of communicating the matter to him, and should be exceedingly thankful to you, sir, for your advice upon the subject. Should it be admitted that this is the cause of the disease, I fear the medical world may seek in vain for a remedy, and I am fearful (if Mr. Hunter should admit this to be the cause of the disease) that it may deprive him of the hopes of a recovery."

Referring to these autopsies at a later time, Jenner wrote to Parry:

At this very time, my valued friend Mr. John Hunter, began to have the symptoms of angina pectoris, too strongly marked upon him and this circumstance prevented any publication of my ideas upon the subject as it must have brought on an unpleasant conference between Mr. Hunter and me.

From the studies and observations, then, of these men originated the correlation of the symptoms of this condition, the introduction of the term "angina pectoris" and the idea that these symptoms had a very definite relationship to coronary sclerosis.

Caleb Hillier Parry was in close association with this group for although he was six years younger than Jenner, they were boyhood and lifelong friends. He at one time spoke of Jenner as a friend of forty years, "acquired in the gay morning of my life." Parry was a famous practitioner of Bath, chiefly known by his account of exophthalmic goiter which antedated both Graves and Basedow. To him Jenner dedicated his work on

Vaccinia. Parry's article on angina pectoris was written when he was 44 and two years before the death of Heberden. This monograph appearing in 1799 was without doubt the best discussion of the subject at that time and, in fact, for many years later. On the title page of the monograph appears the following: "Inquiry into the Nature and Causes of the Angina Pectoris as they are Deducible from the Actual Symptoms and from Dissection." He then writes in his introduction: "Such an inquiry will unavoidably involve me in the necessity of pointing out what appear to me the mistakes of some of my medical brethren in their nosological judgment of this disease. In a personal view this is a disagreeable task but when I consider that truth is the sole foundation of moral and religious virtue and therefore of happiness, my regard to personal delicacy is lost in a more general and greater obligation of public utility. In reality it is of little importance who is the discoverer of truths, however valuable. To mankind it suffices that the truth is actually known and the good obtained." One might add here that Parry gives Jenner full credit for the suggestion that angina pectoris arose from some heart changes, probably ossification or some similar disease of the coronary arteries.

There was a very important observation by Allan Burns published in 1809. This suggested the idea upon which the theory of intermittent claudication is based and the theory which is now quite generally held, namely, that the pain of angina pectoris is due to a relative ischemia. In his observations on "Diseases of the Coronary Arteries and on Syncope Anginosa" he speaks of the effect upon the leg of the application of a tourniquet, which would prevent satisfactory circulation, namely, the early fatigue of the muscle below the ligature. He likens that to the inelastic and incompetent coronary arteries and suggests it as a cause of the pain of angina.

After this publication of Burns there appeared to be no outstanding observations or publications about the coronary arteries until the time of Latham, 1845. This is the more remarkable because that was the period of the distinguished group of Irish clinicians, among whom were Adams, Cheyne, Colles, Corrigan, Graves and Stokes.

Latham was at one time physician to St. Bartholomew's, but gave up the position on account of his health. Later he published a book—"Diseases of the Heart"—based on his hospital lectures. Stokes said of this: "The two concluding lectures of Dr. Latham should be carefully studied, not only as bearing on the disease in question, but as fine examples of medical writing." These last two lectures of Latham just missed being epoch making. Much that he wrote cannot be paraphrased without a definite loss of picturesqueness and charm of expression and in consequence will be quoted:

> Angina pectoris from the time it was first described by Dr. Heberden has always had a large share of attention paid to it. Much has been written about it, and well written, by some of the best men in our profession. But it is still of very doubtful

pathology; and its pathology has little chance of being further illustrated, unless there be a clear agreement among us what we are to understand by the thing itself. . . .

I believe that the definition, which has been given, includes all that is proper to angina pectoris and excludes all that is not; and that it consists essentially of pain in the chest and a sense of approaching dissolution. Not from the absolute constancy but from the very great frequency of its occurrence there is one more element, which has a claim to be considered almost as a part of the disease. Its very peculiarity forces it upon our notice. It is an extension of the pain to one or both arms, most frequently to the left and stopping at the elbow, sometimes to the right, and sometimes to both, and sometimes reaching to the fingers.

But what is angina pectoris? Its symptoms, striking and definite as they are, do not carry their own interpretation along with them. They tell neither whence they are nor what is their efficient cause. . . . (To that end) we must gain what help we can from the many circumstances which various clinical histories and various dissections have disclosed and there are plenty of such histories and dissections upon record. I have both seen many and read many. But all the cases which one sees or reads of a particular disease do not necessarily add to our knowledge. They may make the knowledge which we have, more familiar without augmenting it. They may freshen our experience without enlarging it. Yet some one case out of many from peculiar circumstances belonging to it may teach us something, which we did not and could not learn from all the rest.

Thus, I have three cases of angina pectoris to report, two falling under my own observation and a third coming to me upon the best authority, which added something at least to my knowledge of the disease.

He then reports three cases in detail. All came to autopsy. One of these was Thomas Arnold of Rugby, who with his father, William Arnold, and his son, Mathew Arnold are frequently referred to as illustrating the familial tendency of the disease. After the detailed accounts of these cases he writes:

Here then are three cases of angina pectoris. In the first we have death in a fortnight; in the second death in ten days; in the third death in less than three hours, from the first seizure. Now circumstances cannot be conceived more favourable than those which these three cases present for ascertaining the connection between symptoms declared in the living, and changes of structure found in the dead. The symptoms were essentially the same in all. They were few and striking and constituted of actions and sufferings which manifestly could, and manifestly did, cause death. They were also uncomplicated, no other symptoms interfering to spoil the simplicity of each case, before death arrived. . . .

There are no cases upon record in which death followed the first accessions of angina pectoris so rapidly, as in those three which I have related. And if the disease essentially proceeds from any material element which morbid anatomy can detect, these were the cases in which to find it. You know what *was* found in these cases. Unfortunately for the success of our inquiry, not the same thing in all. Extreme muscular attenuation in two, and muscular attenuation of less degree conjoined with ossified coronary arteries and an ossified aorta in the third. But had there been simple ossification of the coronary arteries in all or simple muscular attenuation in all, yet could neither one nor the other be regarded as the proper efficient cause of angina pectoris. For though one or both are often traceable among the complex forms of disease found in those who die at later periods, yet one and both are often entirely absent. What then have these cases, so new and interesting in their details, taught us after all? . . . They have taught us that angina pectoris has a greater, an earlier, and more instantaneous power to kill than it was ever hitherto thought to have, and they

have (in this way) enlarged our knowledge of its clinical history, and have thus enabled us perhaps better to understand its real nature.

One cannot escape the conviction that these three unusually rapidly fatal cases so well described and discussed by Latham were what is now so easily and often recognized as coronary thrombosis. His differentiation from the angina of effort of Heberden was complete. He even went so far as to put them in a class by themselves and only failed in that he failed to discover the fundamental condition which made them different. Knowing the ease with which thrombosis in a coronary artery may be overlooked, this failure is easy to understand.

In Stokes' book on "Diseases of the Heart and Aorta" in 1854, a book of 600 pages, he allows 8 pages for the discussion of angina pectoris. Most of that discussion refers to the ideas of Heberden, Parry and Latham. He writes:

> Upon the whole, we may conclude, that the special group of symptoms described as angina pectoris by Heberden, Parry, Percival and Latham, is but the occurrence, in a defined manner, of some of the symptoms connected with a weakened heart. *Obstruction of the coronaries may or may not be present, and is probably not infrequent; but as the cause of angina, its action is remote, and its existence unnecessary.**

Major, in his "Classic Description of Disease," gives the credit to Adam Hammer for having first made the diagnosis during life of coronary thrombotic occlusion. Hammer was a German who apparently for political reasons left Germany after the revolution of 1848 and came to this country and, with some associates, established a medical school here. Briefly, the case which Hammer reports and which was reported in *Wiener Medizinishe Wochenschrift*, 1878, was as follows: He was called by one of his younger colleagues to see a patient who was apparently in extremis, and after consideration of the history, the symptoms and signs, he told his colleague at the bedside, that these symptoms could only be produced by thrombotic occlusion of at least one of the coronary arteries. The colleague replied, "I have never heard of such a diagnosis in my whole life" and Hammer writes: "I answered, 'Nor I also.'" Subsequent autopsy showed that the right sinus of Valsalva contained a thrombus which had ultimately completely shut off the lumen of the artery.

This, however, is not at all the type of occlusion which is now so commonly seen in which the thrombus is formed somewhere within the course of the artery, and which is usually due to arterial disease. To George Dock in 1896 has long since been given the credit for having observed and discussed a case of this type and having ventured the diagnosis while the patient was living. He saw the patient about a week after the onset of cardiac pain. His description of the onset and the history at that time was about what one notes now in an ordinarily severe case. The sounds were faint but clear. There was a loud double friction sound at the apex region. There were loud moist râles in the lungs. After giving an

* Italics not in the original.

account of the symptoms and signs, he writes: "The diagnosis was myomalacia following coronary sclerosis with secondary pericarditis. This was based on the history of increasing dyspnea and heart pain without evidence of disease in the lungs or kidneys, or other (valvular) disease of the heart, the history of the acute attack indicating infarction, and the acute onset of pericarditis without other cause." The same day against orders the patient got out of bed to go to the toilet and suddenly died. The autopsy showed a thrombosis of the descending branch of the left coronary and a resulting infarct.

Osler's "Angina Pectoris and Allied States," a volume of lectures delivered in 1896, is rich in references to the symptoms and pathological findings of coronary artery disease, and it is not easy to understand why the correlation of these signs, symptoms and findings was not made earlier. For example, in discussing the coronary arteries and speaking of the descending branch of the left coronary artery, he says:

"This anterior branch is the important one in the morbid anatomy of the coronary arteries, since it is by far the most frequently found seat of extensive sclerosis or of embolism or thrombosis. It may be called the *artery of sudden death.*" He writes further on—"The effect of plugging of the artery is the production of what is known as an anaemic infarct, a well-recognized pathological condition, the consideration of which need not detain us. A very important matter relates to the effect of plugging of the coronary arteries upon the heart-beat; the contractions become of the type known as fibrillary, and it is difficult or impossible to get the organ to resume the ordinary coördinated beats, though experimentally this has been done, even after fibrillary contraction has been established."

In demonstrating a pathological specimen, he said: "In this anterior coronary artery you see a firmly adherent thrombus, which completely occludes the descending branch, to the lumen of which it is firmly attached. It was taken from a man about fifty years of age, who had mitral-valve disease and had a good deal of cardiac dyspnoea. Early one morning he was seized with a severe pain about the heart and shortness of breath, and died in a very few moments . . . no doubt the sudden death was due to the blocking of the anterior branch of the left coronary artery by the thrombus.

"When the occlusion has persisted for any length of time before death the condition of anaemic necrosis may be found. . . . The man with a fresh thrombus in the anterior branch of the left coronary artery probably died in a paroxysm of angina, but he had not had previous typical attacks. As I will tell you later on, the affection is rare in hospital practice so that we do not have opportunities of making the inspection of the bodies of persons who have died of the disease." With reference to its rarity in hospital practice he elsewhere said: "During the ten years in which I lived in Montreal, I did not see a case of the disease either in private practice or at the Montreal General Hospital. At Blockley (Philadelphia Hospital) too, it was an exceedingly rare affection. I do not remember to have had a case under my personal care. There were two cases in my service at the University Hospital. During the seven years in which the Johns Hopkins Hospital has been opened, with an unusually large 'material' in diseases of the heart and arteries, and with many cases of heart pain of various sorts, there have been only four instances of angina pectoris. You will find the statement in Fagge's Practice (third edition, vol. ii, p. 26) that 'the writer has never seen classical angina in hospital practice.'"

In a large consultant practice it was more frequently seen. For instance, Dr. Balfour at that time had analyzed 98 cases which came under his observation in 10 years. Osler said that his own experience had embraced a series of 60 cases, 40 of which he considered to be true angina.

The views and arguments currently put forward as to the reasons for the real or apparent greater frequency of coronary thrombosis at the present time will not be discussed here.

The mechanism of instantaneous death has always been a problem and a problem which has had much discussion and various explanations. Latterly we have come to believe that in many cases in which death in coronary artery disease is instantaneous it is due to ventricular fibrillation. So long as 40 years ago when these lectures were written, Osler made a significant suggestion in speaking of Kronecker's coördination center, of which the "knowledge is still very indefinite." He said:

"I have seen Kronecker perform the experiment, and certainly when the point in the dog's heart is pricked—it is situated about the lower limit of the upper third of the ventricular septum—the organ becomes paralyzed in a state of fibrillary tremor, from which it does not recover. This point is within the area of distribution of the anterior coronary artery, the vessel oftenest found plugged by thrombus or embolus in cases of sudden death."

In another lecture he says, "It does not fall to the lot of many physicians to witness the sudden death in angina but there are observations to show that the pulse beat and the heart stop abruptly. Dr. Thayer (who was present in one instance) tells me that the death seemed instantaneous—the pulse ceased *at once* and there were no further heart beats. As I have before remarked, the mode of death resembles that produced by Kronecker's heart puncture."

In still another lecture speaking of these cases of sudden death, he said, "An explanation of the awful suddenness . . . is probably to be found in the arrest of the heart in fibrillary contractions such as take place experimentally in animals after ligation of a coronary vessel."

Osler describes two cases under the heading of "Rapidly Repeated Attacks of Angina over a Period of Days or Weeks, with the Development of a State of Cardiac Asystole." These he apparently considered belonging in the class of status anginosis. One lived six days, the other 19. The perusal of the history leaves no doubt in the mind of the reader that these two cases were instances of coronary thrombosis. He remarked that he had seen but two cases of this type.

In discussing Allan Burns' Theory, he said:

"Very different to this relative ischaemia of the cardiac muscle must be the condition following the blocking of a large branch by a thrombus or an embolus.* The resulting anaemic infarct, if at all extensive, must cause not alone great weakness of the cardiac muscle, but at the site of the lesion the smooth uniformity of the waves of contraction must be seriously interrupted. This cardiomalacia may lead to rupture of the wall of the ventricle (eleven cases in Huchard's collection of autopsies) *or may cause pericarditis.*† While the anaemic infarct is a well-recognized lesion in fatal

* In this sentence Osler differentiates between angina pectoris and coronary thrombosis.
† Italics not in the original.

cases of angina pectoris, it must be remembered that a paroxysm of pain is really a rare complication of this not infrequent change. It is interesting to note that the scars of infarcts have been found years after recovery from attacks of angina."

Again we have an illustration of how long a time it sometimes takes for a well established medical fact to be recognized and accepted. It is no doubt true that in Latham's time, postmortem examinations were not nearly so carefully made. Pathological processes were not so easily recognized or so well understood but we know that at the time of Osler's writings, these processes were well understood and that autopsies were carefully made and that Osler was an extraordinarily well trained pathologist and clinician. While Osler put these cases of coronary thrombosis in a group by themselves, his experience with them at that time was so limited that it apparently seemed to him as it did to many others for a number of years that thrombus formation in a coronary artery with a resulting infarct was simply an incident in the course of coronary disease which, as a rule, immediately preceded death and was not of particular importance clinically. This in the face of the fact that he makes the definite statement that healed infarcts were frequently found post mortem.

It was another 16 years before Herrick's observations were published indicating that thrombosis may occur and recovery take place with subsequent years of satisfactory life. So far as the clinical diagnosis of sudden thrombotic obstruction of the coronary was concerned, it remained for Herrick to bring order out of the confusion. In his paper of 1912 he described most of the symptoms which we now recognize as being associated with thrombosis: persistent pain, ashy pallor, sweating, nausea, vomiting, abdominal symptoms which might be confused with abdominal surgical conditions, râles in the lungs, arrhythmia, feeble pulse, dyspnea, cyanosis, pericarditis, fever, as well as some changes in the electrocardiogram. This paper was read before the Association of American Physicians, published in the *Transactions* and also in the *Journal of the American Medical Association.* However, scant notice was taken of the subject even then until after his second paper, six years later, in which he reported more cases and emphasized again what he had before published. His observations and suggestions did much to take the condition out of that group of fatal diseases in which the diagnosis is only of academic interest, for he emphasized particularly the opinion that many cases of thrombosis were mild and that recovery frequently did take place. From that time interest in the subject became gradually more widespread until familiarity with the disease became quite universal.

After all, the more familiar one becomes with angina pectoris and coronary thrombosis, the more one realizes that—*if we are right in the prevailing theory of what angina pectoris is, namely that it is due to the relative ischemia of the heart muscle*—these two conditions would seem to be but different manifestations of the same thing, having as their common basis

coronary artery disease. In one the obstruction develops slowly, is progressive, but is partial, while in the other it is sudden and complete. The latter condition is a very common termination of the former. The important reason for their differentiation is that the two conditions require very different treatment. Probably in no other malady does the failure to make a correct diagnosis so frequently contribute to a fatal outcome, as in coronary thrombosis.

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AN ARTICLE CONTRIBUTED TO AN ANNIVERSARY VOLUME IN HONOR OF DOCTOR JOSEPH HERSEY PRATT

EFFECTS OF TREATMENT ON RADIUM AND CALCIUM METABOLISM IN THE HUMAN BODY *

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IN 1924 Blum, a dentist,[1] and in 1925, Hoffman [1] suggested that radium produced necrosis of the jaw. Our knowledge of the pernicious effects of stored radium salts in human beings dates essentially from the publications in 1925 of Castle, Drinker and Drinker [2] and also Martland [3] when necrosis of the jaw in workers who had absorbed radium salts was reported and discussed. Since that time, increasing numbers of similar cases have been recorded. Other abnormal clinical results of radium have been the appearance of severe anemias as well as a high percentage of osteogenic sarcoma, first described and discussed by Martland,[3] in 1931.

In the intervening years, several interesting investigations have been reported regarding the storage and excretion of ingested radium salts, and have been summarized by Evans.[4] Thomas and Bruner [5] gave radium chloride subcutaneously to eight rats. These animals developed a secondary anemia and the bones subsequently showed a hyperplastic bone marrow in the middle of the shaft while an aplastic marrow was found toward the epiphyses. We found a similar appearance in the bones of one human case (C. I.). Only 25 per cent of the injected radium was found in their animals after an average of 21 weeks of injections, followed by 57 days of rest. Approximately 50 to 65 per cent of the injected radium was eliminated one week after the first injection, whereas later average elimination of radium, established for two of the animals, was estimated to be 0.6 per cent per week.

Schlundt and Failla [6] in 1931 studied radium excretion in humans and found that over 90 per cent of radium taken by mouth is eliminated within five days—yet the daily rate of excretion long after exposure was but a small fraction of the total still stored in the bones.

In 1926 a new treatment of lead poisoning was recommended by Aub and Minot,[7] based on the observation that lead in the body parallels the calcium metabolism, and utilizing the available methods of influencing calcium in the bones to control the circulation of lead. In 1929, Flinn and Seidlin [8] reported that such "deleading" therapy with parathyroid extract caused an increased excretion of radium. In 1931, Flinn [9] reported excellent re-

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sults with the use of large doses of viosterol. No collection of excreta was made, but electroscopic tests of the patient were made both by gamma ray method and by radio-activity of the expired air, according to the method described by Schlundt, Barker and Flinn.[10]

These findings of Flinn's were questioned by Craver and Schlundt,[11] who studied four radio-active girls. They were given a low calcium diet and injections of parathyroid extract starting with 10 units every other day and increasing to 50 units a day. They were then given three weeks of high calcium diet with viosterol up to 30 drops a day, followed by three weeks of low calcium diet plus parathyroid extract, and then again given a high calcium diet with viosterol. Only the last three days of each period were analyzed. The results showed an increase of radium excretion in all the analyses with low calcium diet plus parathyroid medication, and equivocal effects from viosterol. They arrived at the conclusion that neither the administration of parathyroid extract nor of viosterol causes a substantial reduction in the total deposited radium.

As with nearly all excellent pioneering work, the technics used in these earlier investigations may be improved. Flinn gave no figures of excretion rate of radium salts. Craver and Schlundt had the patients prepare their own diets and collect their excreta in their homes, but also alternated low and high calcium diets, which reduces the influence of the treatment on stored heavy metals subsequent to the high calcium diet. Neither the parathyroid extract nor the viosterol was adequate greatly to increase calcium excretion; indeed, the viosterol was given probably only as an aid to calcium absorption.

Because of these divergent results, and because of the greatly improved methods available to us, both in metabolic technic and radium analyses, we decided to reinvestigate this problem of radium excretion and of the treatment in cases of stored radium.

Methods. The three patients were put on our routine metabolic regime,[12] and were kept in the hospital during their study. The preparation of their diets and their general management was done with the greatest possible accuracy. Collection of their urine and feces was repeatedly checked in our usual routine manner. The patients were most coöperative, and ate their full diet daily, and there were no known errors made in the collection of excreta throughout their stay in the hospital. The urines for three days were measured and mixed, and an aliquot preserved with hydrochloric acid for calcium analysis. The preparation of the remainder of urine for analysis of radium was the entrainment reaction used by Fairhall[13] for the precipitation of lead, which was found effective for the separation of radium. The precipitate of alkaline phosphates was subjected to wet digestion by nitric acid, dried, and extracted with hydrochloric acid. The entire feces for each period were mixed and digested on the steam bath with nitric acid until a clear solution was obtained. This extract was used for both radium and calcium determinations.

Calcium determinations were made by the method of Fiske and Logan.[14] Radium determinations were made by the method of Evans.[15] Determinations of total radium in the body, as well as expired air samples and blood samples were also made by his methods.[16] The chemicals used disclosed no measurable evidence of radio-activity except the nitric acid which contained not more than 1.5×10^{-12} gram of radium per 100 c.c., an amount which would not affect the results of our analyses.

The excretion of radium has been shown to be very rapid at first and then eventually to settle down to a very small excretion which is but a small part of the remaining stored radium. Schlundt [6] found that when he drank radium in water he excreted over 90 per cent of the radium in the subsequent five days. Seil, Viol and Gordon,[17] and Schlundt, Nerancy and Morris [18] found that the elimination of soluble radium salts was rapid the first week after injection but decreased to less than 1 per cent per day in the next few weeks. In two chronic cases, 12 years after exposure, Schlundt and Failla [6] found an excretion of only 0.002 to 0.005 per cent per day, or about 0.1 per cent per month. High initial excretions were also obtained in rats by Thomas and Bruner.[5] These findings are well confirmed in our observations. One of our patients (Pt. 3—R. L.) had inhaled radium only seven weeks before entering the hospital. Though he was harboring only about 4 per cent of the amount that is stored in our more chronic cases, yet his rate of radium excretion was approximately six times greater than theirs and had been even higher three weeks previously (table 4). The explanation for this appears to depend largely upon the distribution of radium in the body. It has been shown that lead,[19] thorium B,[20] polonium,[21] and radium,[5] itself, are scattered through the soft tissues as well as in the bones soon after administration. In the case reported by Cameron and Viol,[22] though they did not analyze bone, radium was still widely distributed in the rest of the organism 3½ months after intravenous injection. Gradually, these abnormal metals are excreted or stored preponderantly in the bones. Recent work by Calhoun, Hudson and Aub [23] has shown a gradual change in distribution in the bone, itself. At first, a heavy metal is stored largely in the bone trabeculae, there being from 10 to 16 times as much per gram in the trabeculae as in the cortex of the bone. During the following months there is a redistribution and the concentration becomes equal in both trabeculae and cortex. Because the cortex is far heavier than the trabeculae, this means that most of the radium is stored in cortical bone. This distribution indicates an explanation for the variation in radium excretion. The wide distribution in soft tissues and then the accumulation in the bones implies considerable circulation in the blood and, therefore, a chance for rapid excretion. The first large storage in the trabeculae (where inorganic salts are readily deposited and also readily liberated), would allow a continued though less rapid excretion. When the radium finally accumulates in the cortex, it is to be expected that excretion would be slow and relatively poorly influenced by therapy.

The Route of Excretion. Seil, Viol and Gordon [17] and Schlundt and Failla [6] showed that 90 per cent of radium is excreted in the feces. Our experience agrees roughly with this figure. We find the radium in the feces varies with that found in the urine, even during periods of artificially accelerated excretion. Thus in patient 3 (R. L.) the fecal elimination is 96 to 99 per cent of the total excretion in all the periods; in patient 2 (E. C.) it is 94 to 99 per cent in all but two periods (19 and 21); and in patient 1 (M. H.) it varies between 88 to 94 per cent. This is a constant value as judged by usual metabolic variations; indeed far more constant than found for other inorganic salts. Lead is largely excreted in feces and nearly all the increase from therapy appears there.[24] Mercury, however, is excreted more in the urine than the feces, though a low calcium diet plus ammonium chloride increases fecal excretion ten fold and urinary excretion only three and one-half times.[25] None of these metals are normal constituents of the body except in minimal concentrations in contradistinction to calcium, which is fairly closely related to them chemically. When stored calcium is excreted, on our low calcium diet without medication, about two-thirds of it appears in the feces, but nearly all of the increased excretion induced by therapy (excepting that produced by thyroid) appears in the urine. Therefore, there is no constant relationship between urine and fecal excretion ratios in different heavy metals. What induces fecal excretion and what part of the intestinal tract is involved is not well known. It has been shown that lead can be excreted in considerable amounts in the bile.[7] Salant and Meyer [26] found that radium excreted in feces came particularly from the liver and small intestines. We have had an opportunity to get some further information in regard to radium and biliary excretion. A patient (C. I.) who had 5 $(\pm 1) \times 10^{-6}$ gram of radium in her body was found at autopsy to have a good many, though light gall stones. The results of the analyses of one-half (1.83 gm.) of the total sample disclosed that there was 0.032 gram of calcium and 0.022×10^{-9} gram of radium per gram of gall stones (table 3). It is thus clear that radium, like lead, may be excreted through the bile into the intestinal tract. The ratio Ra : Ca is lower in the gall stones than in the bones (see table 3), which may be accounted for by the relatively small concentration of radium and hence only a partial precipitation in bile. Obviously, this does not permit a quantitative interpretation of the concentration or rate of radium excretion.

From these observations, it appears that radium excretion is analogous to that of lead and that (1) approximately 90 per cent of excreted radium appears in the feces, both with normal and stimulated excretion and (2) that some of the excreted radium occurs in the bile, for radium was found in the gall stones of a patient with radium poisoning.

Results of Treatment. The problem of the treatment of radium poisoning was studied in three individuals who had received their store predominantly by different routes: (1) intravenous, (2) by mouth, and (3) by inhalation. Two of the patients represented chronic effects with obvious

symptoms, while the third had only recently absorbed a small amount of radium without deleterious effects.

Case Reports

Patient 1. (M. H.) had received an undetermined amount of radium intravenously ten years before entrance to the hospital. This was given as therapy for a minimal amount of chronic arthritis, which had not subsequently progressed. On admission she was suffering from severe necrosis of the jaw of two years' duration. Eight months before entrance she had devoted six weeks in her home to a low calcium diet plus ammonium chloride and thyroid extract. Therefore, this was her second course of treatment, and it is to be expected, from our experience with lead, that the results obtained in the hospital would be of lower magnitude as a result of this previous therapy. At the end of her hospital stay, she had 15.2 ($\pm$ 1) micrograms of radium stored in her body. This was determined by adding 8.5 micrograms of radium determined as radium C gamma rays plus 6.7 micrograms found as radon in an analysis of expired air (1.7×10^{-10} Curies of radon per liter) (table 5).

Table I

Patient 1, M. H. Total Radium in Body = 15×10^{-6} gm.
(Intake and Output in 3-day periods)

Period	Diet and Medication			Calcium in Serum	Calcium Excretion	Radium Excretion	
					Urine	Urine	Feces
				mg. %	gm.	$\times 10^{-9}$ gm.	$\times 10^{-9}$ gm.
1	Low calcium diet only (0.27 gm. Ca)			9.9	0.45	0.17	2.5
2				9.8	0.39	0.16	2.1
	Thyroid extract	NH_4Cl	Parathyroid extract				
	gr.	gm.	units				
3	9	18	1200	11.3	0.32	0.37	2.5
4	9	18	900	10.3	0.51	0.60	4.9
5	9	18	1200	11.3	0.56	0.27	5.5
6	9	18	1500	11.8	0.28	0.99	8.4
7	9	19.5	1500	11.5	0.96	0.82	7.2
8	9	22.5	1500	12.2	1.68	1.94	
9	9	22.5	1200	13.1	1.40	1.70	16.4
10–11	9	22.5	1200				
12–13		18	1200				
14		18	1200	12.5	0.92	0.78	8.2
	Second Admission—After 5 weeks on low calcium diet						
15	High Ca diet (5.0 gm. Ca)			10.0	0.16	0.34	2.5
16	Diet plus Ca gluconate (10.0 gm. Ca)			11.0	0.52	0.21	2.3

Without medication she excreted an average of 0.8×10^{-9} gram of radium per day which is about 0.005 per cent of her total body radium. From the laboratory data as disclosed in table 1, it is clear that the use of a low calcium diet plus ammonium chloride, plus thyroid and parathyroid extracts [7] increased her radium excretion six to eight fold during the period of maximum medication.

The control period, obtained five weeks later, corresponded to the original output of radium. It must be pointed out, however, that the rate of excretion of these chronic cases of radium poisoning is of an extremely low magnitude. In spite of the fact that this medication definitely increased the radium elimination, the total increase remained but a small fraction of the total radium which was stored in her bones, for she only excreted approximately 0.1 microgram more than would have been eliminated without this therapy. This represents an increase of only two-thirds of 1 per cent above her normal rate (0.15 per cent) of elimination per month. Yet there was a striking improvement in the condition of her mandible. Before treatment, the necrosis of bone had progressed during two years to such an extensive bone destruction that her very able dentist had told her not to yawn for fear that she would fracture her jaw. Following this therapy, the sinuses in the bone promptly disappeared and the bone healed into a respectable and quite normal-looking jaw.

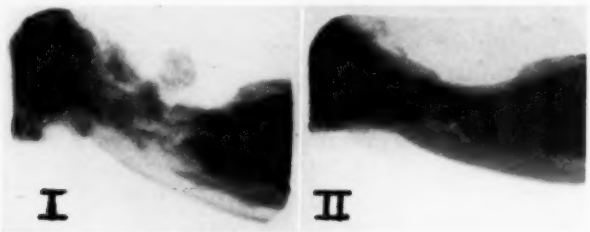

FIG. 1. Roentgenograms of the same area of mandible of Patient 1 (M. H.). I. Taken before treatment, showing necrosis of mandible. II. Taken nine months later, and one month after second course of treatment.

The roentgen-ray photographs indicate this striking change. (Figure 1.) In the two years which have followed this observation, this condition has continued well, except for a single, very small and superficial spicule of bone which remains in the gum. This striking improvement occurred in spite of the fact that only a small percentage of the total radium stored in her body could have been eliminated during the course of this treatment.

Patient 2. (E. C.), a woman of 30 years, was a dial painter from the time she was 16 years of age. From her industrial surroundings it is obvious that most of the radium which she had stored was accumulated in the first seven years of her exposure, and that in the last seven years exposure must have been slight. This is based upon the fact that cleanliness of the

factory was greatly improved, and the technic of applying paint was changed from mouth-pointed brushes to the use of sharp glass pencils. The evidence for early accumulation of radium in this patient is also shown in her bones.

From roentgen-ray pictures it may be seen that obvious damage had been done before the epiphyses at the head of the humerus and the femur had united, with the result that this area of the bones shows distinct lesions

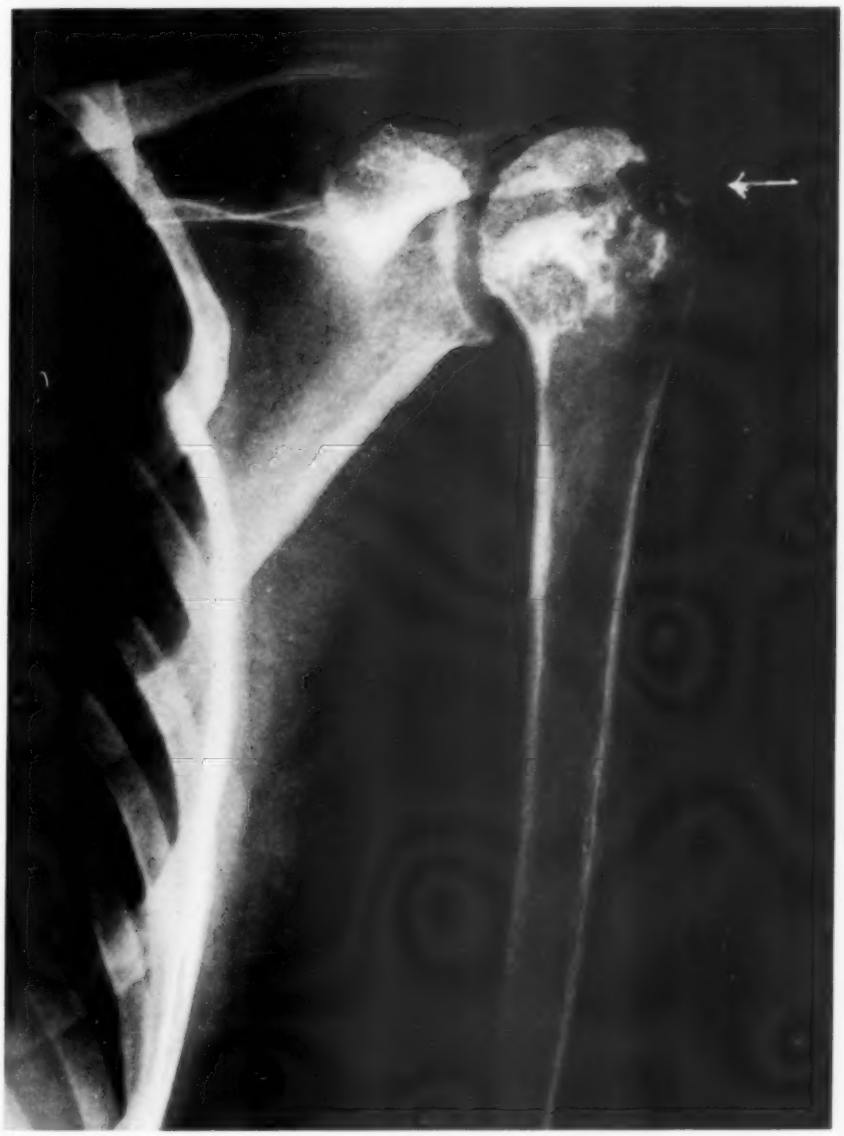

FIG. 2.

FIGS. 2, 3, and 4. Roentgenograms of Patient 2 (E. C.). These disclose the abnormal epiphyses, and varying degrees of bone destruction and proliferation.

and abnormal union. (Figures 2 and 3.) It is well known as a result of the observations by Vogt [27] and Park,[28] and our own analyses [29] that the heaviest deposit of lead in the bones of children is at the epiphyses. It is

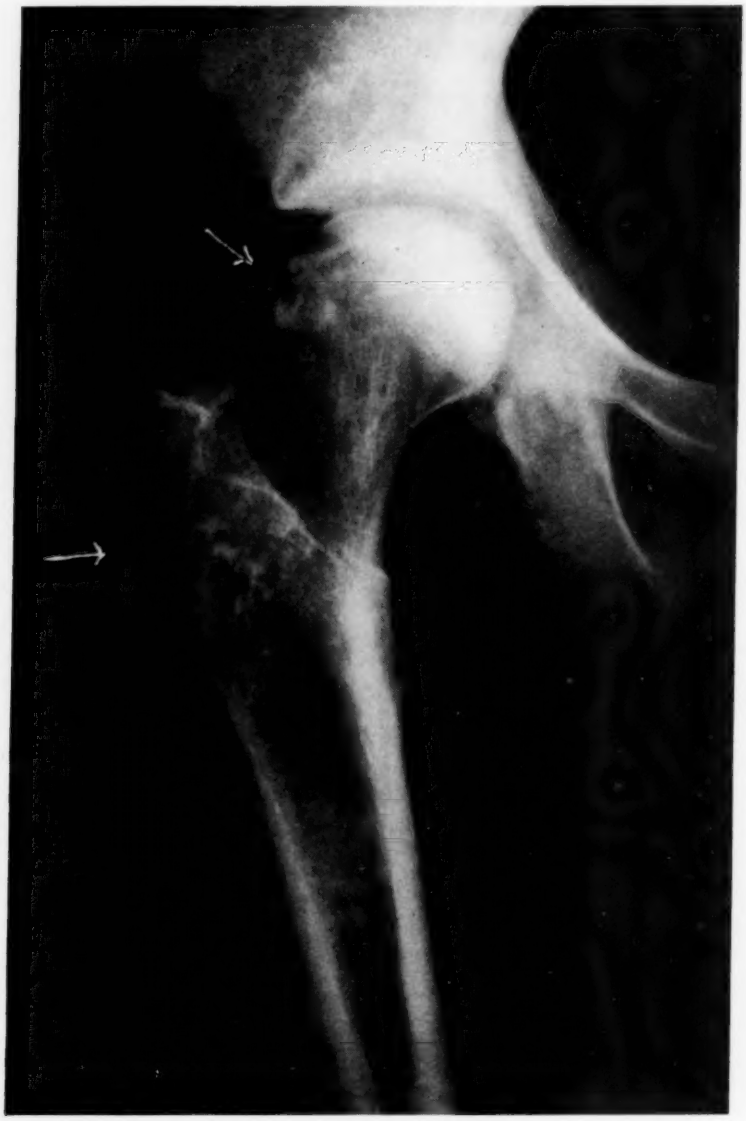

FIG. 3.

highly likely that radio-active salts have a similar predilection for epiphyseal areas, because in rats they are also the areas most heavily impregnated with thorium in the observations of Behrens and Baumann [20] and with radium as judged by the picture published by Thomas and Bruner [5] (their figure 15).

This is also true of radio-active lead in dogs.[23] It, therefore, seems quite clear that the bone lesions in this patient represent deleterious radium effects obtained from a high concentration of radium in the ununited epiphyses. As the upper epiphyses of the humerus normally unite at 20 years of age, and of the femur at 18 years, one must expect that its effect occurred before this age.

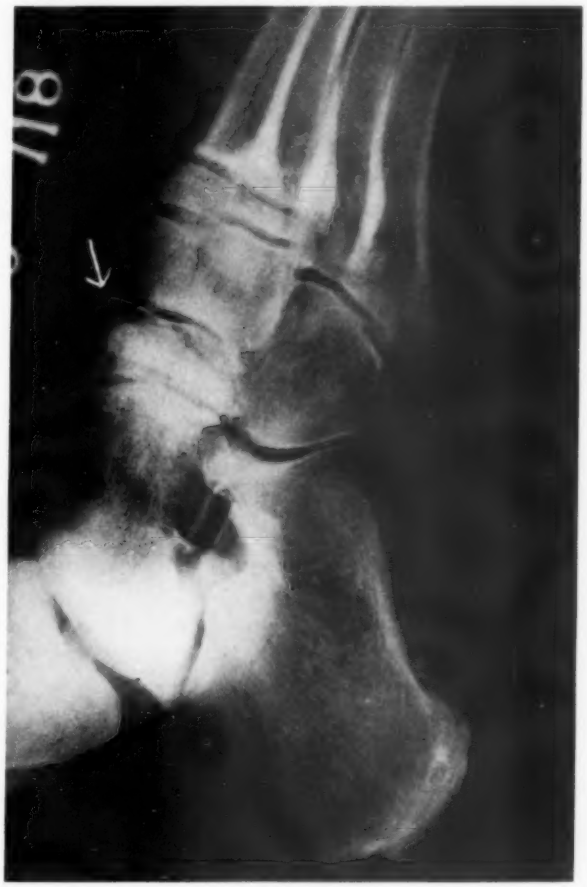

FIG. 4.

Here, then, is a patient who had been exposed to radium for 14 years, with most of the exposure in the first seven years. The deleterious physical effects which she manifested obviously dated back to this early exposure. One cannot say, however, that she was entirely free from exposure during the last seven years. Very careful calibration of the radium in her body disclosed that she had 18 $(\pm 1) \times 10^{-6}$ gram of radium stored in her body. Gamma ray measurements indicated that the radium was distributed non-uniformly, in the manner characteristic of radium poisoning.[16]

This patient was an excellent subject for metabolic study, for she co-

TABLE II

Patient 2, E. C. Total Radium in Body = 18×10^{-6} gm.
(Intake and Output in 3-day periods)

Period	Diet and Medication				Serum Values		Calcium Excretion		Radium Excretion	
					Ca	P	Urine	Feces	Urine	Feces
					mg. %	mg. %	gm.	gm.	$\times 10^{-9}$ gm.	$\times 10^{-9}$ gm.
1	House diet								0.07	2.7
2	House diet								0.17	2.7
3	Low Ca diet only (0.31 gm. Ca)				10.2	4.6	0.22	0.29	0.04	2.8
	Thyroid ext.	NH_4Cl	Parathyroid ext.	Mg gluconate.						
	gr.	gm.	units	gm.						
4	6	12					0.47			3.9
5	6	15	750				0.47	0.19)		5.9
6	6	15	900		10.1	2.7	0.46	0.20)		5.5
7	9	15	1500		10.3	2.4	0.54	0.17		5.9
8	9	15	1500		10.1	3.3	0.72	0.14		6.2
9	12	15	1800		9.9	3.5	0.63	0.12)	0.25	5.8
10	12	18	2100				0.79	0.11)	0.35	6.8
11	12	18			9.6	3.4	0.61			8.2
12	12	18			9.6	3.6	0.70	0.10)	0.52	8.1
13	12	18					0.79	0.10)		10.2
14	12	22.5			10.0	4.1	0.71			6.8
15	12	22.5					0.74	0.14)	0.53)	14.4
16	12	22.5					0.84	0.15)	0.53)	10.0
17	12	22.5		51	10.0	3.9	0.81	0.21		10.8
18	12	30		51	9.6	3.6	0.87	0.21		10.6
19	12	30		51	9.9	3.7	1.07	0.15	1.40	9.9
20	12	30		76.5			0.97	0.27	0.62	12.0
21	12	30		76.5			0.96	0.21	0.86	9.3
22	Low calcium diet— No medication						0.40		0.28	9.4)
23							0.19	0.15	0.22	9.4)
24					10.2		0.14	0.16	0.13	(7.6
25							0.14	0.17	0.11	(7.6
26	Ergosterol— 6 drops						0.17	0.14)	0.15	
27	Ergosterol— 9 drops				9.9	5.4	0.17	0.14)	0.13	
28	Ergosterol— 9 drops				10.0	5.9	0.15	(0.09		9.4)
29	Ergosterol—10 drops				10.5	5.6	0.18	(0.08	0.15	9.4)
30	Ergosterol—12 drops				10.5	5.4	0.23	0.05)		8.2
31	Ergosterol—18 drops				10.2	5.6	0.30	0.05)	0.19	7.6
32	Ergosterol—30 drops						0.29	(0.04	0.15	7.3
33	Ergosterol—30 drops				10.2	6.1	0.27	(0.04	0.25	10.0
34	Low Ca diet only				10.2	6.0	0.34	0.03	0.25	8.7
35	High Ca diet only (4.1 gm. Ca)				10.7	5.9	1.46	lost		
36							1.42	1.72	0.15	6.3
37					10.2	6.0	1.26	1.77	0.24	4.1
38					9.9	5.2	1.25	2.18	0.16	5.6
39							1.21	2.06	0.12	4.0

Bracketed figures represent combined analyses.

operated very well in every way. We were, therefore, able to obtain a very complete and accurate metabolic observation. For the first two periods she was on a normal house diet, and at this time her normal rate of radium excretion was determined, and found to average 0.9×10^{-9} gram per day which is approximately 0.005 per cent of the total radium in her body. From then on the course of her metabolic studies is indicated in table 2.

The results of the observation indicate that the various metabolic procedures which we used caused an increase in radium excretion roughly parallel to the calcium excretion. A low calcium diet, plus thyroid extract, and the acid-producing salt, ammonium chloride, definitely raised the radium excretion just as it did in Patient 1, and throughout the various periods of medication the radium excretion remained between three to four times the control values.

The addition of magnesium gluconate to therapy was accompanied by a slightly increased amount of ammonium chloride in order to partially neutralize the alkaline magnesium gluconate. In spite of the reduced acidity of this regime, both radium and calcium excretions were elevated by the magnesium gluconate, and this was the only therapy which seemed to increase the relative proportion of radium excreted in the urine. This finding corroborates the similar finding of Tibbetts and Aub [30] of the effect of magnesium ingestion on calcium excretion.

The radium excretion, however, does not always parallel the change in calcium excretion; thus in the periods of no medication (23 to 25), the calcium excretion had returned to a very low level, but the radium excretion continued relatively high. In the last four periods (36–39), in which a high calcium diet was given, in spite of a definite storage of calcium at that time, the radium excretion still remained well above its original level. This may be accounted for by the fact that vitamin D has a metabolic effect which certainly lasts a month. The fact remains, however, that the excretion of radium varied much more sluggishly than that of calcium. This may well be due to the fact that heavy metals, when liberated from bone, are stored in various soft tissue organs such as the liver, lungs, and kidney. When such a storage occurs, one would expect an elevated excretion to continue just as it does in acute cases.

Several other phenomena occurred in this observation which are of importance. This patient did not respond at all to very large doses of parathyroid extract (Lilly), either in the blood calcium level or in the rate of calcium excretion. This can be seen by comparing the calcium excretion in periods 8 to 10 with that in periods 11 to 16. Nor was there any dramatic change in radium excretion during this medication, inasmuch as the radium progressively increased in excretion throughout periods 6 to 16. We are certain that this batch of parathyroid extract was potent, for it was retested on dogs both by Eli Lilly Company and by us, and a satisfactory elevation of blood calcium was obtained. Why then did this patient not respond except by a slight lowering of blood phosphorus level? A possible

explanation is that her osteoclasts were sufficiently damaged so that they were unable to respond to the normal stimulus of parathyroid extract, and were, therefore, unable to liberate bone salts. Further evidence of damage to bone cells is suggested in this patient by the low level of phosphatase in the blood stream (normal is 0.15 Kay units) which would suggest that the osteoblasts were relatively inactive. The phosphatase determinations of this patient (0.06 Kay units) did not vary throughout the observation. In spite of this suggested injury to her bone cells, however, this patient was still able to store calcium at a rapid rate in the first periods of high calcium diet toward the end of her observation.

Another medication to which there was no dramatic response was very large amounts of activated ergosterol, of which she was given as much as 750,000 international units in three days, without effect on her blood calcium level. The only response to these high doses was a shift in her calcium excretion from feces to urine, indicating an increased absorption of calcium from the bowel. The storage or liberation of calcium in the bones was not affected. However, this cannot be said to be definitely abnormal in spite of the big doses, because C. I. Reed [31] also did not get constant changes in blood levels from similar doses, but it is suggestive evidence confirmatory of that obtained with parathyroid extract. All that can be said of its effect on radium excretion is that this remained at the higher levels (table 2) established by the previous therapy. In summary, one may say that the methods of therapy which we used did increase the rate of radium excretion but the amount of radium which was withdrawn in this advanced case was insufficient to definitely lower the determinations of total stored radium in the body. In this regard the results agree with our first case and with the conclusions of Craver and Schlundt.[11]

Is Radium as Easily Excreted as Calcium? It would be of interest to know whether the radium which is excreted corresponds with its relative ratio to calcium in bone, in order to determine whether therapy is more efficient in eliminating either the normal body constituent, calcium, or the abnormal radium. What one wants to know is the Ca : Ra ratio in the bones as compared to the excreta. The ratio as it appears in the excreta may be estimated from two groups of periods during a constant low calcium diet, in which the excretion of *extra* calcium and radium must come from the bones. If one compares the metabolic periods 5 to 10 with periods 18 to 21, in this case, one finds an increased calcium of 0.43 gram and radium excretion of 4.7×10^{-9} gram per period. From our calcium analyses of bone (0.233 gram of calcium per gram of dried bone), 0.4 gram of calcium represents approximately 1.7 grams of bone, which would indicate that this patient had an approximate radium content of 2.8×10^{-9} gram per gram of bone.

The radium concentration in the bones of this case can be estimated in three other ways: (1) By actual analysis of two bone samples, which were necrotic trabeculae spontaneously extruded from her jaw, we found 19.6

and 13.6×10^{-9} gram of radium and 0.212 and 0.230 gram of calcium per gram of bone.

TABLE III

Analyses of Dried Bone and Gall Stones

Patient	Area	Wt. of Dried Bone analyzed	Calcium per gm. of dried bone	Radium per gm. of dried bone
		gm.	gm.	$\times 10^{-9}$ gm.
	Spicules from gum	0.301	0.230	13.6
No. 2—E. C.	Spicules from gum	0.075	0.212	19.6
C. I.	Fibula—Trabeculae	0.403	0.200	1.75
	Fibula—Shaft	1.164	0.238	1.63
	Tibia—Trabeculae	1.172	0.239	0.86
	Tibia—Trabeculae	1.849	0.255	1.30
	Tibia—Shaft	2.620	0.246	1.06
	Tibia—Shaft	3.357	0.256	1.79
	Vertebrae	1.219	0.242	2.38
	Gall stones (Total wt. app. 3.7)	Wt. of gall stones analyzed gm. 1.834	Calcium per gm. of gall stones gm. 0.032	Radium per gm. of gall stones $\times 10^{-9}$ gm. 0.022

Calculating from this ratio, the actual increase in radium excretion during therapy is about one-fifth that which one would expect from the increase in calcium excretion. However, it has been shown that bone areas vary distinctly in their radium content and the mere fact that this bone was composed of trabeculae and had been killed justifies the assumption that it was relatively high in radium content. (2) The average radium in bone may be estimated, however, from the known radium stored in them. If one assumes the bones to be 16 per cent of the total body weight (53 kg.), and, knowing the total radium stored (18×10^{-6} gram), one obtains the average figure of only 2.1×10^{-9} gram of radium per gram of bone. (3) The average bone radium may be calculated from comparison with another case, in whom total radium and actual bone analyses were obtained. In this case (C. I.), who had approximately 5 (± 1) $\times 10^{-6}$ gram of radium in her body, the average analysis of five bone samples (table 3) gave 1.53×10^{-9} grams of radium and .239 gram of calcium per gram of bone. By correcting this ratio for the greater total radium storage of our patient 2 (E. C.) the average radium content of her bones would be 5.4×10^{-9} grams of radium per gram of bone. With calculations as crude as these, it appears that this figure roughly corresponds with the calculation of bone radium concentration obtained from the excreta and from calculation 2 above. These results, and similar calculations on patient 1, suggest that excreted and stored Ca : Ra ratio roughly correspond. The conclusions may, therefore, be drawn that the methods employed here are not more efficient in extracting radium than in extracting calcium from bone. It is more likely that they are both excreted in their relative proportion in the body—though possibly the calcium is slightly more easily mobilized.

Patient 3 (R. L.) was a physicist who had inhaled a very small quantity of radium only seven weeks before admission to the hospital. The radium storage when he started the metabolic studies represented only 0.6 ($\pm$ 0.1) $\times 10^{-6}$ gram of radium, yet this patient who had only about $\frac{1}{25}$ of the radium present in the other two patients was excreting radium at a much more rapid rate than were they. During the first period on metabolic regime, he excreted 1 per cent of his stored radium per day. This agrees with Schlundt's observations that the early excretion of radium is at a rapid rate in comparison to the excretion after several years.

TABLE IV

Patient 3, R. L. Total Radium in Body 0.6 $\times 10^{-6}$ gm.
(Intake and Output in 3-day periods)

Period	Diet and Medication			Serum Calcium	Calcium Excretion		Radium Excretion	
					Urine	Feces	Urine	Feces
				mg. %	gm.	gm.	$\times 10^{-9}$ gm.	
Preliminary (4 weeks after accident)								45.0
First Admission to Metabolic Ward—7 weeks after accident.								
1	High calcium diet			10.6			0.28	18.0
2							0.32	15.0
3							0.27	11.5
	Low calcium diet (0.33 gm. Ca)							
	Thyroid Extract	NH_4Cl	Parathyroid Extract					
	gr.	gm.	units					
4		9		10.8	0.59		0.21	10.0
5		12	750		0.69	0.34	0.22	10.0
6		12	750	11.6			0.24	10.0
7	3	15	900	11.9			0.24	11.0
8	3	15	900	11.6			0.23	12.0
9	3	15	1200	11.9	1.24	0.36	0.23	9.3
10	3	15	1200	11.6	1.25	0.38	0.22	12.7
Second Admission—24 weeks after accident.								
11	High calcium diet			10.6			0.05	1.5
12							0.05	1.2

The rate of radium excretion was obviously falling very rapidly before medication was started, a decrease which one would expect to progressively

continue. The medication which we were able to give this patient was never large in amount and could be increased only slowly because of his sensitive, nervous make-up. The result of the medication was to raise his blood calcium approximately 1 milligram, but we did not produce an acidosis, inasmuch as the CO_2 content of his blood at the end of treatment was 22.3 millimeters per liter (low normal equals 25 millimeters) and the pH of his blood at that time was 7.4.* We, therefore, must assume that the therapy that this patient received was only moderate, and the effect on his radium excretion was to prevent a further decrease and, in fact, to initiate a slight increase in excretion (table 4).

When one considers the very moderate effect on the *calcium* excretion produced by medication and the very low Ra : Ca ratio in the bones (because of the small amount of stored radium) one should expect that the increase in radium excretion would be negligible. As a matter of fact, if the reasonable assumption is made that the continued fall of radium excretion seen in the control periods would be progressive, then the effect of therapy on the radium excretion is striking and of a far greater magnitude than that found in the chronic cases. This is further brought out by the markedly reduced excretion found approximately three months later, when the total radium content of his body had fallen to so low a level that it could not be quantitatively measured from gamma ray observations.

Alveolar Air and Blood Concentrations. Samples of normally expired air were obtained from all three of the patients at various times. The numerical results are given in table 5.

All radium slowly disintegrates spontaneously into the radioactive gas, radon, which has a half-value period of 3.8 days. It is noteworthy that in each of the cases studied about 45 per cent of the total radon produced by the decay of stored radium escapes continuously from the body through the lungs. This fact indicates the intimate nature of the contact between the circulating blood and the stored radium (which is located almost exclusively in the bones.) Specimens of approximately alveolar air were also collected and analyzed for radon. The technic of these collections and analyses has been previously described.[16] Table 5 shows that the radon concentration in the alveolar air is about two or three times that of normal expired air. As one would expect, there is no significant change in the breath radon values during the course of medication. No therapy would affect the production of radon, and its blood concentration and excretion by lung would be dependent upon the various gas laws.

It naturally becomes of interest to determine the radium content of the blood. The radium analytical technics are sufficiently delicate to permit approximate analyses of 5 c.c. of blood, though somewhat erratic values of blood radium were obtained. From a series of analyses, there seems to be slightly less radium in the red blood cells than in the serum. The blood of patient 2 (E. C.) was repeatedly analyzed and showed a mean value of the

* We take this occasion to thank Professor Baird Hastings for these analyses.

order of 1×10^{-12} gram of radium per c.c. of blood. Assuming a total volume of 5 liters of blood this is 5×10^{-9} gram of radium in the blood, or only about 0.03 per cent of her total body radium (18 micrograms).

TABLE V

Measurement of Gamma Rays in Body and Radon in Breath

Patient	Period	Gamma Rays	Breath	
			Normal	Alveolar
		10^{-6} g. Ra (as Ra C)	10^{-10} Curie/liter	10^{-10} Curie/liter
No. 1—M. H.	2		1.66	
	6		1.71	
	9		1.34	
	11		1.67	
	One month after medication	8.5 (±0.5)		
No. 2—E. C.	1	10.0 (±1)	1.9 (±0.1)	
	3	9.7 (±1)		
	9			3.6 (±0.05)
	10		2.1 (±0.05)	
	13		2.0 (±0.1)	
	21		4.3 (±0.1)	
	24	10.0 (±1)	3.8 (±0.2)	7.2 (±0.1)
	38	11.0 (±1)	2.6	7.7
No. 3—R. L.	Preliminary	0.25 (±0.1)		
	Preliminary	0.50 (±0.1)		
	2	0.33 (±0.05)		
	3		0.030	
	4		0.043	0.053
	5		0.044	0.055
	7			0.036
	7			0.066
	9			0.056
	12	0.15 (±0.1)		0.034

Even knowledge of the approximate order of magnitude of the average radium concentration in the blood allows us to make several interesting calculations. Blood specimens taken from patient 2 (E. C.) during period 24 show an average of 0.95×10^{-12} gram of radium per c.c. of blood. This was a period of relatively low urinary radium output, but will serve for calculation. The kidneys eliminated 0.04×10^{-9} gram of radium per day during this period. As the blood supply to the kidneys is at least 500 liters per day,[32] the blood stream carried an equivalent of $5 \times 10^{5} \times 0.95 \times 10^{-12} = 5 \times 10^{-7}$ gram of radium; therefore, less than 0.01 per cent was removed continuously from the blood stream and eliminated from the body. Only about 1 per cent of the radium in the blood stream at any one time was removed per day. This computation emphasizes the relative ineffectiveness

of the kidneys in removing radium (and possibly other heavy metals) from the blood stream.

During this period 24, the fecal elimination was 2.5×10^{-9} gram of radium per day, or 60 times the urinary elimination. Considering the vastly greater blood supply to the liver and gut we can say that the overall permeability of these organs to radium appears to be of the same rough order of magnitude as for the kidney. During period 18, the blood radium averaged 0.5×10^{-12} gram of radium per c.c., while the fecal elimination was 3.5×10^{-9} gram of radium per day. Here a similar calculation shows the daily elimination to be slightly greater than the total blood radium content at any moment of the day. These rough approximations suggest that it is less difficult to get radium out of the bone and into the blood stream than it is to get radium out of the blood stream and into the excreta.

Discussion

From these observations, one may get a fairly clear-cut picture of what happens in radium poisoning. In the acute stage, during the first few months after exposure, the radium is scattered through the body and obviously more loosely held than later, and is therefore excreted at a far more rapid rate. In the later stages the bones hold onto the radium more tightly than at first. From the observations of Calhoun, et al.,[23] it is obvious that soon after heavy metals have been absorbed the trabeculae of bones have a relatively high concentration to that present in the cortex, while as time goes on there develops a more even distribution. Due to the relatively great amount of cortex, it is obvious that the greater proportion of radium is eventually stored in this part of bone. Inasmuch as it has been shown that the trabeculae are readily available for mobilization, and inasmuch as the radium is at first widely distributed in the organism, this gives a partial explanation of the relatively large liberation in the early weeks. As time goes on, it is to be expected that the cells should be injured or even killed in the area where radium is stored, and that the bones would respond less effectively to medication directed toward influencing their metabolism. In the patients we have studied, however, there has been a definite response to such medication, though in these chronic cases this has not been of a magnitude to greatly influence the total radium stored. Yet in spite of this relatively small percentage rise of radium excretion, a dramatic recovery from bone necrosis followed therapy in one of the patients (Patient 1 (M. H.)). Whether this was a matter of chance will remain a problem until further accumulation of evidence. It is obvious that such an improvement is only apt to occur when patients are treated relatively early before bone cells may be sufficiently injured so that recovery cannot take place. It remains for further studies to show whether this clinical improvement in this late case was due to a redistribution of radium in the bones, by largely dissolving trabeculae such as surround the teeth.

Conclusions

Radium stored in the body is analogous to lead in distribution, mode of excretion, and relationship to calcium metabolism.

When radium is absorbed before the union of bone epiphyses, this area of bone may appear abnormal.

Most stored radium (more than 90 per cent) is eliminated in the feces even when the excretion is artificially stimulated.

The bile contains radium, and therefore also appears to be a route of excretion.

Radium excretion can be elevated four to eight fold by decalcifying therapy, but this still does not greatly reduce the total stores of radium in the body.

The response of radium excretion to deleading therapy is slower than is the calcium response. The excretion rate rises slowly and is prolonged after therapy has stopped. The probable mechanism involved is discussed.

The administration of magnesium gluconate appears to elevate radium excretion just as it affects calcium excretion.

One case of advanced, chronic radium poisoning gave no response to large amounts of parathyroid extract, possibly because of damage to bone cells. The only response to activated ergosterol was to maintain a high level of radium excretion. Nevertheless, storage of calcium was still accomplished when a high calcium diet was administered.

The rate of increased radium and calcium excretion, after the effects of therapy have been established, indicates that the efficiency of treatment is roughly the same for both, and it is probable that the average Ca : Ra ratio present in bone is approximately similar to that of the stored metals excreted.

Case Histories

Patient 1 (M. H.) was a woman of 54. About 10 years before entrance she was given an unknown amount of radium intravenously for arthritis. Neither the number of injections nor the amount of radium can be ascertained. There is also the possibility that she drank a little "radium water." Thirty-two months before entrance, she had a left lower molar tooth removed, and after this her jaw never healed and subsequently had to be repeatedly curetted. A year later the few remaining teeth were removed, and the entire left lower jaw was curetted. This continued not to heal, and spicules of bone continued to appear until eight months before entrance, when stored radium was found but was not quantitatively determined. At that time she had six weeks' treatment with low calcium diet and daily oral administration of six grams of ammonium chloride and two grains of Armour's thyroid extract. After this treatment she returned to a high calcium diet. The chronic area in her jaw promptly improved, but was still draining in November 1934, when she entered the hospital for further treatment.

Physical examination was essentially negative except for necrosis of her jaw. She remained in the hospital until December 15 on therapy outlined in her table then returned home and remained on a low calcium diet, but without further medication until she was readmitted to the hospital on January 16, 1935. She was then given a high calcium diet, and in addition 8 grams of calcium gluconate daily, and the last control observation was then made.

A roentgen-ray of the jaw on January 30, 1935, showed considerable filling in with new bone which had occurred within the last eight weeks. Since this time her jaw has progressively improved. The sinuses stopped draining within two months, and for the last year the bone has had a practically normal appearance.

All the laboratory results were normal except that the red blood count was 3,900,000, though the hemoglobin was 91 per cent (Sahli). The plasma phosphatase on entrance was 0.12 Kay units (average normal value 0.15), and 0.20 Kay units after therapy was discontinued.

Patient 2 (E. C.) was a 30 year-old woman, who entered the hospital complaining of painful feet on walking. Just 14 years ago, when she was 16 years old, this young lady began painting luminous numbers on watch dials, and since then she has been almost continuously employed in the same work. For the first seven years the brush was touched to the lips to point it for the delicate work. For the past seven years the painting has been done with glass pens, and under far better hygienic conditions. Five years ago, she began to notice aching in the right ankle when walking, and two years ago the right foot was put into a plaster jacket for one year. One and one-half years ago, the pain started in the left hip. Four years ago she first had trouble with her jaw. It became swollen and three teeth were subsequently pulled, and the upper jaw remained swollen for several months thereafter. It did not really subside for six months, with continuous drainage since that time in both upper and lower jaw. These sinuses have produced very little pain. Five months ago a tooth dropped out of the right upper jaw spontaneously. The patient's diet was adequate but she rarely drank milk. About six months before entrance, radium was first detected in her body.

Her physical examination appeared normal except the jaw which showed a small area of exposed bone in the right upper area, and also a loose piece of cancellous bone between teeth in the left upper jaw. There was a very small draining sinus in the left upper jaw.

Four days after her admission she lost a small piece of cancellous bone from the right jaw. The second piece, which was very loose on entrance, came away after a month in the hospital, and the third very small piece from the same area came away three weeks later. There did not seem to be any other loose bone about her teeth. The bone pains practically disappeared after she had been in the hospital several weeks, but before her discharge they returned in about the same intensity as on entrance.

Her stay in the hospital was without untoward incidence, except that on the forty-second day after admission she complained of right-sided abdominal pain, a little nausea, and loss of appetite. This was possibly a mild attack of appendicitis, but it promptly subsided without therapy. Her study was continued for 18 weeks, and she left the hospital in excellent condition.

Extensive laboratory studies were all negative save for an anemia of 3,600,000 with 63 per cent hemoglobin (Sahli) which developed while she was in the hospital. This was completely relieved within a month following iron and liver therapy. There were a surprising number of stippled cells seen in all of her blood smears, sometimes more than one in each field. The roentgen-rays of bones showed interesting small areas of rarefaction and eburnation scattered through the trabeculae. There was distinct pathological union of the epiphyses of shoulders and hips, indicating a definite radium influence before epiphyseal closure. The treatment and pertinent laboratory studies are shown in the table. Plasma phosphatase was consistently low throughout her stay in the hospital, being 0.06, 0.07, and 0.06 Kay units.

Patient 3 (R. L.) was a physicist (male), 54 years of age. Fifty-three days before entrance he was sealing a mixture of 100 milligrams radium chloride and 5 grams of beryllium powder into a steel tube when the plug was blown off this tube and some of the mixture filled the room. Some particles settled on his face. While still in the laboratory he washed himself carefully, but it is probable that he breathed

some of the dust at this time. He promptly thereafter had his eyes and teeth carefully cleaned. There have been no symptoms following this exposure to radium. The patient is well except that he had had indigestion for several years prior to five years ago, when an appendectomy was performed. Since then his digestion has improved.

Physical examination was not abnormal.

The patient was maintained on a high calcium diet for three periods, during which time he was allowed to eat what he pleased, except for a daily ration of one quart of milk. He was then put on a carefully weighed low calcium diet, and started at the same time on 3 grams of ammonium chloride a day. The subsequent medication is indicated on his table. Until his discharge 30 days after entrance, the patient continued on a very moderate amount of medication because he was afraid his old indigestion would be reprecipitated, and therefore only mild doses of medication could be used. Careful laboratory studies were all normal. He had no anemia, and his blood phosphatase determination was also normal, being 0.14 Kay units on entrance.

He then went to Europe for the summer, remaining on a rather low calcium diet. He had excellent health all summer and spent much of his time mountain climbing. After 12 weeks he returned to the hospital where he remained for seven days. During this period of observation his radium excretion was measured for control purposes, while he was given a full diet with added milk. It is interesting that he had gained 11 pounds in the 10 weeks between the two hospital admissions.

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AN ARTICLE CONTRIBUTED TO AN ANNIVERSARY VOLUME IN HONOR OF DOCTOR JOSEPH HERSEY PRATT

GONORRHEAL ENDOCARDITIS WITH BILATERAL PAROTITIS AND TOXIC JAUNDICE AS ADDITIONAL COMPLICATIONS *

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THE first case of gonorrheal endocarditis in which the gonococcus was grown by blood culture, as well as by cultures from thrombi on the heart valves, was reported by Drs. Thayer and Blumer [1] in 1896, in the Johns Hopkins Hospital Bulletin. Previously, there had been a few cases in which the organism found in endocarditis was morphologically and tinctorally characteristic of the gonococcus. It was also intracellular in the smear made at autopsy. Since then, cases presenting this complication in gonorrhea have multiplied, until in 1932 Hoffman and Taggart,[2] after a careful review of Thayer's list [3] of reported cases, rejected six of them and added seven more, including one of their own, so that at that time 76 instances of this condition were found to have been reported. More recently, additional cases have been reported, for Eakin [4] in 1934 found two more, increasing the number to 78, and in the years that have followed more have been published, so that now about 150 reputed cases have been recorded. In 1934, Stone,[5] after a careful analysis of all of the reported cases, divided them into four groups totalling 123 cases. He allotted to the first, or proved group, 85 cases; to the second, or presumptive group, 12 cases; to the third, or probable group, 15 cases; and finally to the fourth, or possible group, 11 cases. In this list he could find only 34 cases in which the gonococcus had been grown by blood culture, although in 71 of the 112 cases falling within the first three groups, blood cultures had been made and in 14 of them, where the gonococcus had not been found by blood culture, it had been grown from the heart's blood, vegetations, joint, pericardial or pleural fluid. Thirteen additional cases [6] have yielded positive blood cultures in the years that have intervened since then. Of course some cases of this condition have existed, and do now exist, from whose blood culture the gonococcus has never been isolated, although numerous attempts have been made to grow it. On the other hand, the organism has been grown by blood culture in cases of bacteremia in which there has been no demonstrable cardiac involvement. Tabbutt,[7] for example, has reported two such cases. Jenkins,[8] O'Brien and Bancker,[9] Wheeler and Cornell,[10] Rubenstone and Israel,[11] Filler,[12] and Friedberg [13] also have reported similar cases with recovery. Others probably exist in the literature upon this subject. The

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recoveries from this condition have been few, but they are not as rare as was formerly supposed. Stone [14] lists six of them, and Newman [15] adds nine to their number. Since then, two more have been reported. Kolle and Hetsch [16] were of the opinion that only 0.7 per cent of all the patients who acquired gonorrhea developed gonococcal septicemia. The portal of entrance of the organism in every case is the genito-urinary tract, although occasionally the primary focus cannot be discovered. The history of our case is as follows:

Case Report

Gonorrheal cervicitis two week following exposure; chills and evidence of cardiac involvement two months later followed in two weeks by recovery of the gonococcus by blood culture after five negative results; typical course of endocarditis with subsequent onset of bilateral parotitis and terminal toxic jaundice.

S. V., female aged 17, worker in the tobacco fields, was admitted to the Hartford Hospital on the Gynecological Service on August 23, 1934, complaining of pain in her right side. This symptom appeared 10 days before, but subsided quickly only to appear again the day of her entrance into the Hospital with nausea but not vomiting. She thinks she had some additional pain, however, at her June period, and may have had some fever on that occasion. Four months ago, about the middle of May, while returning with her partner from a dance, she was violently attacked by him and raped. Fourteen days subsequently a profuse yellowish vaginal discharge was noted. Her period, after the attack, came on two days later and continued for five days. Previously it had always been regular every 28 days, and of two to three days' duration. Now she is a few days over-due, and is much concerned about it, fearing pregnancy. She thinks that in the past month she has not felt as well as she normally does, and that occasionally she has had sensations of chilliness and fever. Her family history and past history were negative.

On admission she was found to be a well developed and well nourished woman, with face somewhat flushed; she was lying comfortably in bed and did not seem ill save for her flushed facial expression; the lungs were negative on examination, while the heart, though not enlarged and with sounds of normal relative intensity, showed at the base in the pulmonic area, a slight blowing systolic murmur. The abdomen was negative save for slight tenderness in the right lower quadrant. By vaginal examination the urethral orifice showed slight reddening with the presence of a slight, milky discharge, while from the vagina a profuse, yellowish discharge was noted. Bi-manual examination revealed slight tenderness in the right lateral fornix. Her temperature on admission was 101.2°, and her leukocyte count 25,200, with the polymorphonuclears 95 per cent and the mononuclears 5 per cent.

On August 27, Dr. Howe made the following note: "Nulliparous type of introitus; profuse thick flocculent discharge; Skene's ducts injected and a thin, milky discharge is readily expressed from them, smears taken. Cervix shows a slight degree of erosion about the external os, otherwise negative. Fundus normal in size and consistency, freely movable with some tenderness; no masses palpated, but patient is acutely tender on the right side. Impression: Acute skenitis, vaginitis, urethritis and endometritis probably Neisserian in origin. Treatment: Rest and expectant treatment." Twelve days later he noted the examination showed no change, save that the tenderness had disappeared but the local condition was unchanged in spite of the daily douches and routine treatment. A blood culture was taken on September 7, and I was asked to see her five days later.

Being on the Medical Service, I thought as her heart and lungs were normal that her pelvic condition might account for the temperature, and advised that she

remain at present on the Gynecological Service. I suggested further blood cultures, as well as a search for malarial organisms. The soft, systolic murmur which had existed at the pulmonic area since admission, did not appear to have any especial significance. Her temperature since admission had shown marked remissions, resembling closely a picket-fence. I advised at a second consultation on September 17, that a culture be taken at the height of her temperature, and again at its lowest point. A cystoscopic examination was performed the next day with negative results. On September 20 she developed marked systolic and diastolic murmurs at the base in the

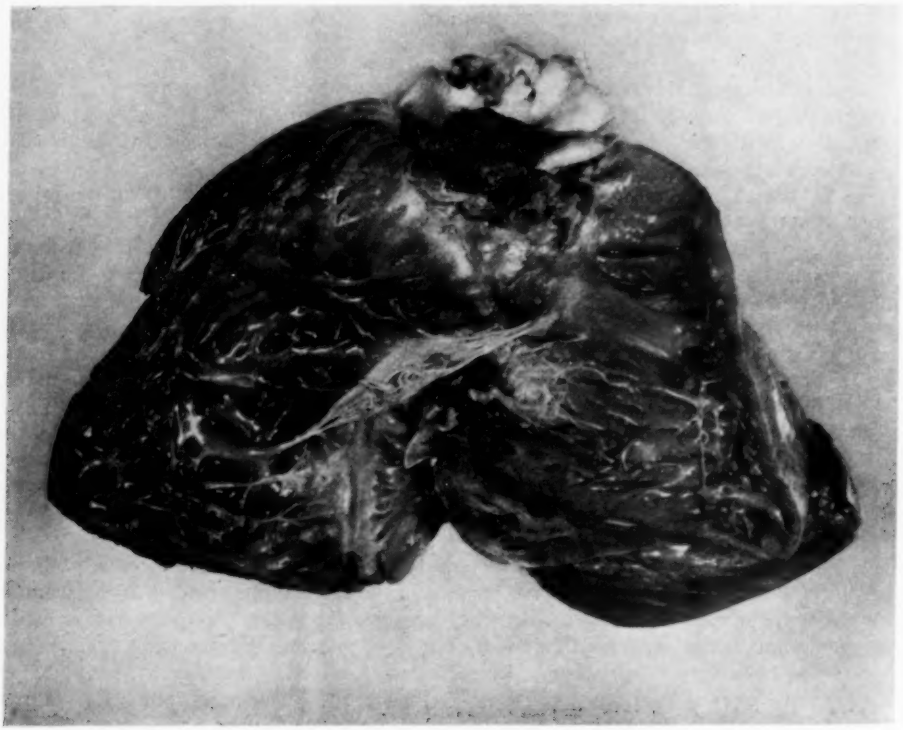

FIG. 1. Pulmonic valves with vegetations.

pulmonic area. Convinced that the septic process was localizing itself on the pulmonic valve, although the blood cultures had been uniformly negative, I accepted her for transfer to my Medical Ward. In spite of five negative cultures, I ordered one of my interns to take another culture, plant it at the bedside and proceed at once with it to the Laboratory. We were shortly thereafter rewarded with the report of a gram-negative diplococcus being found, which was culturally and morphologically typical of *Neisseria gonorrheae*. In the culture from which it was isolated there were approximately 9 colonies per c.c. of blood. Some weeks later, on October 24, another successful blood culture was obtained with approximately 80 colonies per c.c. of blood. The patient was given twice weekly transfusions of 250 c.c. of blood, with no improvement (14 in all). The febrile excursions became less marked, but the chills, which were first noted on September 20, continued. After this first one, they were daily for three days, then after a five day interval, daily for seven days, and subsequently after one or several days interval continued daily until her death. A severe and intractable cystitis developed about October 15, which nothing seemed to

relieve. About this time she complained of pain in the left upper quadrant, but the spleen was not palpable until November 9. Eleven days later a bilateral parotitis was observed, which quickly responded to cold applications. The patient now became increasingly somnolent, was often irrational and was at times a difficult nursing problem. The murmurs at the pulmonic area became much more pronounced; she developed a toxic jaundice with bile in her urine and died on November 28.

Laboratory Data: Urine: August 24, 1934. Yellow, clear, no sediment, acid, specific gravity 1.010. Albumin, none; sugar, none; microscopically, a few white blood corpuscles. A month later a few hyaline and granular casts were seen, the white blood corpuscles showed an increase and some red blood corpuscles were noted. The white blood corpuscles soon became more numerous and showed distinct evidences of cystitis by their numbers, singly and in clumps. The specific gravity varied from 1.009 to 1.025. Bile was found in the urine on November 25, 1934. The non-protein nitrogen on October 10 was 33 mg. per cent but by November 21, it had risen to 70 mg. per cent. *Blood:* The leukocyte count on entrance has been given. By September 3, it had fallen to 9,100, while the differential count showed: Polymorphonuclears 79 per cent; lymphocytes 19 per cent; mononuclears 2 per cent. On September 14, the hemoglobin was 60 per cent and the red blood corpuscles 3,650,000. A week later the hemoglobin had fallen to 56 per cent, while the white blood count was 13,450, with the following differential count: Polymorphonuclears 92 per cent; lymphocytes 6 per cent; mononuclears 2 per cent. There was slight anisocytosis present. In the next month, on October 16, there was not much change save in the white blood count which had risen to 19,200. The hemoglobin and red blood corpuscles showed slight change until the end, but the white blood count fell on November 10 to 10,900.

Electrocardiograms: Were made on September 26 and October 8. Dr. Robert S. Starr, our cardiologist, made the report on both of them. The first showed a pulse rate of 105 per minute, with normal rhythm; P. R. interval 0.14 second. Impression: a normal E. K. G. In the second, the only difference was in an increased pulse rate, it being 120 per minute.

Cultures: Blood. Four blood cultures were taken on September 7, 13, 17, 19 and 21 with negative results. Finally, one was taken on September 28 and brought quickly to the laboratory. It showed a gram-negative diplococcus culturally and morphologically typical of *Neisseria gonorrheae*, with approximately nine colonies per c.c. of blood, while another on October 18, showed a similar organism in larger numbers, 80 colonies being seen approximately per c.c. of blood.

Urine: The urine showed on September 17 the *Staphylococcus pyogenes aureus*, the *Streptococcus hemolyticus* and *non-hemolyticus* and the *B. fecalis alkaligenes*, but on October 19, only the *Staphylococcus pyogenes aureus* and the *Streptococcus non-hemolyticus* were grown. Five smears from the cervix and urethra were taken and were negative for gonococci.

An autopsy was performed by Dr. Perry Hough two hours after death. The anatomical diagnosis was *gonorrheal cervicitis; gonococcus septicemia; acute pulmonary gonococcus vegetative endocarditis; acute splenic tumor; chronic passive congestion of the kidneys* and *jaundice.*

There was a marked icterus of the skin and conjunctivae, besides small, irregular petechiae which were scattered profusely in the skin over the upper and lower extremities. The changes in the lungs, heart, spleen and kidneys merit full description, and were as follows:

Lungs: Right 350 gm. Left 300 gm. There are no adhesions and no appreciable amount of fluid in the pleural cavity. On section there is practically no edema or congestion. Scattered throughout both lungs, especially in the lower lobe, there are a few dark, nodular areas, appearing to be small areas of infarction, and in the base of the right lower lobe there is one wedge shaped area of infarction just outside of the

periphery about 1½ cm. in diameter. There is no pneumonic consolidation. The bronchi and peribronchial lymph nodes appear normal.

Heart: 240 gm. There are about 80 c.c. of cloudy, amber fluid within the pericardial cavity. The right ventricular wall is 4 mm. in thickness, the left ventricular wall is 15 mm., and there is a marked dilatation of the right side of the heart with less dilatation of the left. The myocardium everywhere appears grossly normal. The aortic, mitral and tricuspid valves are grossly normal. The leaflets are thin, and vellumentous, with no vegetations. The pulmonic valve is markedly involved with large, varicose, buff-colored, friable vegetations extending completely around the ring, involving all of the leaflets. The largest averages 2 cm. in diameter and is attached by a broad pedicle. There are smaller, nodular, similar vegetations extending for about 2 cm. along the pulmonary artery and scattered diffusely over the endocardial surface of the right ventricle in the region of the pulmonic valve. The coronary arteries are thin and patent throughout.

Spleen: Tremendously enlarged, weighing 1100 gm. and extending 9 to 10 cm. below the left costal margin. Splenic notch is preserved. On section the organ is moderately firm and dark red in color. The malpighian corpuscles are rather indistinct and at one point toward the lower pole there is a small, somewhat lighter area than the surrounding tissue of slightly increased density, possibly representing a small infarct. It covers a diameter of approximately 1 cm.

Kidneys: Weight together, 420 gm. Capsule thin, and strips easily, leaving a smooth cortical surface over which there is scattered diffusely tiny areas of hemorrhage, averaging less than 1 mm. in diameter. On section the cortex is swollen. Tiny hemorrhages are seen throughout the cortical tissue and the normal striations are somewhat indistinct. Renal pelves and ureters are grossly normal, as is the bladder.

Genitalia: Negative, save for a few tiny cysts in the upper and posterior cul-de-sac of the vagina, averaging 1 mm. in diameter. The tissue is here moderately indurated.

Microscopic Examination:

Lungs: Microscopically normal except for the areas of infarction mentioned in the gross. These microscopically appear to be typical infarcts with degeneration of the alveolar walls, the alveolar spaces being engorged with blood cells, serum and old blood pigment. In one section, apparently from one of the old infarcts, there is complete necrosis. Around the margin there are a few polymorphonuclear leukocytes, and interspersed among these there is a suggestion of bacteria having a coccus form but not being definitely biscuit-shaped diplococci.

Heart: Section of the heart valve shows superimposed upon it a vegetation consisting of well organized thrombus in which many proliferating fibroblasts are seen along with a few polymorphonuclear leukocytes and a moderate small round cell infiltration. Special stain reveals through the vegetation colonies and isolated groups of gram-negative diplococci microscopically typical of gonococci.

Liver: Essentially negative.

Spleen: Splenic sinuses are engorged with red blood cells and throughout there is an accumulation of brown pigment, apparently old blood pigment. There is no increase in the reticulum elements. The malpighian corpuscles are rather small and somewhat distorted. No areas of infarction are seen microscopically.

Kidneys: The tiny hemorrhages mentioned in the gross appear microscopically to be only dilated capillaries engorged with red blood cells and old red blood pigment. There is no actual hemorrhagic extravasation in the renal parenchyma. There is cloudy swelling of the tubular epithelium. The glomeruli everywhere appear normal. No interstitial fibrosis or red cell infiltration. A few tubules, however, contain casts composed chiefly of degenerated blood. No gonococci found by postmortem culture.

Genitalia: No evidence of acute inflammatory reaction in the sections from the

vagina. The epithelium in one portion has been denuded apparently at the site of one of the small cysts mentioned in the gross. Underlying the epithelium there is a slight infiltration with small, round cells. Cervix: Presents a similar picture. The epithelium is everywhere intact, but beneath this there is a definite layer of chronic inflammatory reaction, consisting essentially of small round cells with a slight degree of fibrosis. Salpinx: Negative.

Summary and Comment

Our patient was a woman, aged 17 years, who developed an acute cervicitis two weeks after the exposure to infection; an endocarditis followed after an indefinite period; followed in turn by a bi-lateral parotitis and a terminal toxic jaundice. The blood culture was positive and the pulmonary valve was found to be involved at autopsy. Since this case was seen, two other methods for the treatment of gonorrhea have been utilized, namely: artificial fever [17] and the drug sulphanilamide. Both seem to offer something in the way of treatment.

Dr. W. S. Thayer [18] has shown that the aortic valve is most commonly implicated in this disease, and that the pulmonary valve is more commonly affected in this variety of endocarditis than in the sub-acute type. Although gonorrheal endocarditis generally follows an arthritis, a study of this case shows that this latter complication was absent. An initial chill probably ushered in the heart involvement. The bilateral parotitis which occurred later in the disease, was probably due to bacteria which were secondary invaders. Jaundice is a rather unusual development and probably had a toxic etiology. It was seen in Silvestrini's case [19] which recovered, and in Blumer and Nesbit's fatal case [20] where it was associated with a hepatitis.

Recently Lichtman [21] has reported a case in the *Journal* of the Mt. Sinai Hospital in which he considers that the jaundice probably resulted from rapid and extensive blood destruction, overactivity of the reticulo-endothelial system and liver cell damage due to bacterial toxins. The presence of bilirubin in the urine indicates a regurgitative type of jaundice associated with hepato-cellular necrosis. Lichtman refers to a former article he wrote in conjunction with Kugel [22] on "Factors Causing Clinical Jaundice in Heart Disease." He also gives a reference to Popper and Wiedman's interesting article [23] on "Gonotoxic Icterus." In our case, the jaundice appears to be due to the effect of the gonotoxin on the parenchyma of the liver. The red blood corpuscles remained about stationary at 3,500,000. Popper and Wiedman consider the jaundice caused by this microörganism generally similar to the simple catarrhal type, although occasionally cases are found resulting finally in acute yellow atrophy of the liver.

The difficulty of cultivating gonococci has caused the number of these cases reported to be comparatively few in their relation to the total published number of cases presenting this complication. A positive ante- or post-mortem culture is, however, the only absolute criterion for a diagnosis. A

history of gonorrhea followed by a mono-articular arthritis which is in turn followed by an endocarditis offers strong presumptive evidence of the endocarditis being gonorrheal in origin. Indeed it would do so even if a mono-articular arthritis had not existed and even though the blood cultures were negative.

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AN ARTICLE CONTRIBUTED TO AN ANNIVERSARY VOLUME IN HONOR OF DOCTOR JOSEPH HERSEY PRATT

THE NON-OPERATIVE TREATMENT OF HYPERTHYROIDISM *

By Dr. Helmut Dennig, *University of Berlin*

Even though, in the present day treatment of hyperthyroidism, operation is more frequently resorted to than is conservative treatment, nevertheless the latter still has a wide field of usefulness which is well worth reviewing. In Germany, opinion is still very much divided concerning the value of non-operative treatment. There are clinics where patients are seldom brought to operation and others which use only operative treatment. The majority probably occupy a middle ground. In this connection, I may refer to the questionnaire which we presented to several clinics a year ago.[1]

A great many misunderstandings have arisen because of the fact that nomenclature is not uniform. Many authors distinguish special forms of the disease, which are, for example, termed " hyperthyroidism " as opposed to " complete Basedow." In America the toxic adenoma plays a special rôle which finds little or no recognition in Germany. It is particularly difficult to define the very mild cases, the transitions between " vegetative stigmatization " to " mild Basedow " or " Basedowoid," etc. In the presence of such confusion, statistics concerning the results of treatment by various authors can hardly be compared. The best conclusions can be drawn if, in the same clinic, some patients are referred for operation and a similar number are reserved for conservative treatment, after which the end results may be compared. My personal experience has such a basis.

We do not deny the possibility that there may be certain special forms of the disease—for example, those of pituitary origin or where the underlying cause is perhaps not an excessive amount of thyroxin, but another unknown toxic substance. The actual proof of the existence of such special forms is, however, not assured. It seems likely to me that in the majority of cases there are no qualitative differences, but only quantitative ones which are of significance. If the illness is frequently variable in form, we need not assume variable noxae, but simply that the same noxa results in different reactions in individuals of different makeups. This is also true in other diseases. In any case, it seems to me entirely satisfactory in everyday practice to speak of mild, moderate and severe forms. Here, the clinical picture, as a whole, must be the deciding factor. Of all the symptoms, the increase in the basal metabolism is probably still the best measuring stick, but it would be unwise to let this be the sole criterion. Cardiac disturbances

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Translation by Robert W. Buck, M.D.

may be of much greater significance. The various symptoms are different, too, in different communities. In Berlin, for example, we see quite a number of patients who have no exophthalmos and little or no enlargement of the thyroid gland, so that the diagnosis is often not made.

One of the first needs which must be met is *psychic treatment,* although I question whether excitement or fright plays such a decisive rôle in the origin of hyperthyroidism as is often assumed. Nevertheless, it is certain that they are very significant in the further progression of the disease. Removal of the patient from the cares of daily life or freeing him from oppressive psychic conflict—for example, by conversation with a good physician—may cause apparent improvement. In this sense, a change in environment often has a good effect, as we see when the patients are brought to a hospital from a sanatorium. Perhaps, in this connection, certain *climatic factors* may be of significance, regions of moderately high elevation being favored. At any rate, certain sanatoria enjoy an especially good reputation, not entirely without reason, and specialize to a certain extent in the treatment of hyperthyroidism. *Physical rest* shares with mental reassurance the task of conserving calories, thereby combating emaciation in the presence of the elevated metabolism. On this account, a great deal of time in bed or even strict bed rest is indicated, at least for a few weeks.

For the same reason, the diet must be rich in calories, disregarding the unusual cases of obese patients with hyperthyroidism. Most physicians prefer a diet poor in protein on the ground that protein elevates the basal metabolism because of its specific dynamic effect. I do not think we need worry too much about this. At any rate, our first concern must be the maintenance and stimulation of the appetite by giving a mixed diet which should be rich in vitamins as well. There are certain definite indications for the administration of vitamin. For example, vitamin " A " is supposed to have a definite effect against hyperthyroidism. Wendt [2] has reported improvement with large doses; I, myself, have not as yet been able to arrive at any definite conclusion in this respect. However, this subject is still open.

Not a few patients have a tendency to *diarrhea.* This is in part the expression of a nervous acceleration of intestinal peristalsis and in part the result of a hypoacidity or anacidity of the gastric juice which is fairly common in hyperthyroidism. In every case of diarrhea, a fractional gastric analysis should be made because, in these cases, very definite improvement may be achieved by a rather careful diet, together with the administration of hydrochloric acid (e.g., acid hydrochloric non-dilut., pepsin sicci, 40.0, aquae q.s. ad 200), 1 teaspoonful in a glass of water, ⅓ of which is to be taken through a glass tube before, during and after the meal.

Insulin and glucose are often prescribed, since in animal experiments a definite antagonism between thyroxin and insulin has been demonstrated. The general effect, however, is only slight. Nevertheless, in the presence of marked emaciation and loss of appetite, a trial is justified. Increase in weight is, to be sure, for the most part attributable to water retention.

Physical and mental rest may be effectively supported by means of *medication.* We give either bromides or, better still, drugs of the barbituric acid series. Luminal has, in general, proved most satisfactory. The dosage, however, must be strictly adjusted to the individual's peculiarities—in many cases, very small doses suffice, perhaps 0.015 gram two or three times daily. Other patients require much more, perhaps as much as 0.05 gram morning and noon, together with 0.1 gram in the evening. If luminal results in drowsiness rather than sedation, prominal should be tried, which has a predominantly sedative effect; approximately double the above dosage may be given. A favorite old-fashioned remedy to improve the general condition is arsenic in practically any form.

A great many of the symptoms of hyperthyroidism rest upon an irritability of the sympathetic nervous system. *Ergotamine* may be regarded as a direct antidote which lowers the excitability of this system. As a matter of fact, many symptoms can be markedly influenced with this drug—those such as tachycardia, tremor and even exophthalmos. However, if sufficiently high doses are given over a prolonged period, the danger of ergotism and gangrene of the extremities is considerable. Further, ergotamine often causes nausea. As a result, I have quite given up its use.

Repeated attempts have been made to discover anti-substances in animal blood which will be effective against the action of thyroxin. In this group belong the old antithyreoidin of Moebius, derived from thyroidectomized sheep, or Blum's thyronorman. Although these investigations are very interesting—in animal experiments the substances seem to be quite effective—nevertheless, in my personal experience I have seen no important practical results. It is possible, however, that further progress may be made along these lines.

Much more effective than the above mentioned methods is *iodine treatment.* Although the pre-operative administration of iodine over short periods of time, as introduced by Plummer and Boothby in 1924, is now recognized throughout the whole world, the prolonged treatment, as advocated in 1920 by Neisser in Stettin, is still disputed. However, our experience during the last few years has also brought a good deal of enlightenment in this connection. This much is certain: treatment with iodine is an art demanding intuition and experience; without these, harm may result. However, in the hands of an experienced man who knows the limitations of the treatment, it is extraordinarily effective. As yet we know very little theoretically as to what happens when iodine is administered and on this account we have had to depend all the more on our experience. This shows us the following facts:

The optimal dose lies between 50 and 200 milligrams of iodine daily; within these limits, individual variations can and should be made. Nothing is to be gained by giving larger amounts. Indeed, a single larger dose may occasionally lead to acute exacerbation of symptoms. The manner of ad-

ministration of iodine is unimportant, only the amount of iodine given being significant, whether or not the iodine is given in organic or inorganic form. Thus, we have seen no difference between calcium iodide, sodium iodide, Lugol's solution, di-iodide thyrosin or sajodin, so long as the above mentioned dosage of iodine was maintained.[3, 4] Frequently, however, by changing the form of the preparations, some of the unpleasant by-effects, such as iodine coryza or iodine acne, may be controlled; however, these by-effects are rare and often must be accepted as part of the bargain.

The favorable effect of iodine occurs after two or three days, reaching its maximum in one or two weeks; the basal metabolism falls sharply, the pulse rate becomes slower and, not infrequently, a completely irregular pulse becomes regular again, tremor grows less, exophthalmos often diminishes, the restlessness disappears and there is a gain in body weight. The great question is only—for how long a period does this improvement persist? The surgeons believe that operation should be performed at the maximum point of this improvement, which is, no doubt, correct in the majority of cases, if operation is to be done in any case. If operation is not performed, however, and iodine is nevertheless continued, the favorable effect gradually diminishes; at least, there is no further continuation in the improvement. It is well to stop treatment from time to time—for example, to give iodine for eight to 14 days and then to stop it for three to five days and to constantly repeat this series. This may be continued over several months. I wish to say very definitely, however, that a complete cure is almost never attained by these methods. As soon as iodine is given up for a prolonged period of time, the old symptoms return; sometimes, indeed, more marked than before. Here lies the danger in iodine treatment. If we once begin to use iodine, we do not dare to stop it unless an improvement is obtained in some other fashion—i.e., either by operation or roentgen-radiation. Further, after a course of iodine of long duration, particularly if intervals of freedom have been observed, one can still operate. In this way, very sick patients may show a marked gain of weight in the course of a few weeks and may be operated upon while in much better general condition. Of particular significance is iodine treatment of long duration in association with roentgen-radiation, which will be discussed below. The good effect of radiation begins only after a number of weeks. During this period patients can be maintained temporarily in very good fashion by means of iodine, which may be given up when the roentgen-ray effect is apparent. This seems to me to be the principal value of long-continued iodine treatment.

There are only a few patients who do not respond to iodine and in practice a trial of its use can be made in the most widely different forms of hyperthyroidism. It has an especially favorable effect in those cases of hyperthyroidism which have been induced by iodine. Even these cases do not, as a rule, occur during the period that iodine is being given (as, for example, in anti-luetic treatment or in arteriosclerosis), but rather more especially

when the iodine is discontinued. It requires some courage to give iodine again if it is known that the condition was caused by giving iodine. But experience shows that we must have this courage and that the patients become much better if we give them iodine again. Then, by all means, however, cure must be effected by operation or radiation.

It is also very important to give iodine if a patient with hyperthyroidism is attacked by an infection or meets with an accident. In this way he can be carried through a dangerous period.

Roentgen-ray treatment is also the subject of controversy. Here, however, the limits of treatment and its indications are gradually becoming clear.* If a good roentgen therapeutist conducts the treatments, it is certainly even less dangerous than operation. Indeed, if radiation, as described above, is combined with intermittent iodine treatment, there is practically no mortality whatever to be considered. This is a great advantage which decisively determines the course of action for many patients and physicians. There are, however, very serious objections to this procedure. The number of complete cures is not nearly as large as with operation. If many authors, however, still deny that any good results follow roentgen-ray treatments, this can only be the result of insufficient experience or unsatisfactory technic. I am familiar with a whole series of severe cases which were completely cured after radiation, but, as a matter of fact, many complete failures also occur and one sees particularly often marked improvement, but no such complete cures as usually occur after operation. After a few months there may be recurrences. Often we can obtain further improvement after a new series of radiations, but the end result still remains less certain. A further objection is the long duration. As a rule, several weeks or often as much as three to five months elapse before the definite improvement begins. During this time very dangerous spontaneous exacerbation of the disease may occur and this is the principal reason why we demand simultaneous iodine treatment as above mentioned.

If no permanent results occur following radiation, not much time or money has been lost. It is possible, in spite of a widespread opinion, even then to operate without any special difficulty, if one has not waited too long. At any rate, I have seen a great number of patients who were operated upon several months after a course of radiation which was without result, and who were then cured.

The symptomatic treatment of *disturbances of circulation* demands

* My personal experiences are based upon patients in my ward, the iodine treatment of whom I have supervised and whose roentgen-ray treatment was undertaken in the wards of Dr. Muehlmann of Stettin and Prof. Frik of Berlin. As a rule, 10 roentgen-ray treatments were given with intervals between them of 8 to 10 days. After the fifth radiation, there was usually a rest of five weeks and the remaining five treatments were then given similarly to the ambulatory patients. A radiation of 185 roentgens, measured in air, 0.7 Cu. half value layer over a large field including thyroid and thymus is given at a distance of 30 to 40 cm. at each treatment so that in a period of ten to twelve weeks a total of approximately 1650 roentgens measured in air are given. The effective dosage in this area is not uniform, but may probably be considered to be in the neighborhood of 1000 to 1100 roentgens measured in air.

special attention. The simple tachycardia of hyperthyroidism, with its markedly short contractions of the heart, and pulsus celer is doubtless an unfavorable form of cardiac activity. While in other cardiac conditions, digitalis slows the rapid pulse, here, for the most part, there is no clear-cut effect. Only when definite circulatory failure with congestion of the liver and edema occur is it desirable to make use of digitalis. As a rule, iodine, alone or in combination with digitalis, works much better. Auricular fibrillation in hyperthyroidism is especially noteworthy. It may be the expression of severe damage to the heart muscle, but frequently is only a transient symptom which is relatively easy to control in contrast to the auricular fibrillation caused by arteriosclerosis. Auricular fibrillation occurs during periods of aggravation of the hyperthyroidism, as for example, during the first few days after thyroidectomy, and during periods of transitory improvement it may suddenly disappear. Quite often the cardiac action becomes completely regular under iodine treatment, but as soon as iodine is omitted, the auricular fibrillation recurs. The irregularity may also, for the most part, be corrected by means of quinidine or quinine, but, as is well known, the use of these drugs is not entirely without danger and should only be carried out by experienced persons with constant clinical observation.

If, then, we search for indications for the various forms of treatment, we shall perhaps take the following position: Very mild cases should perhaps not be treated at all, particularly not with iodine—they should be only watched. These are the patients who have single mild symptoms, such as tachycardia, or vasomotor excitability with a tendency to profuse sweating, or a slight stare, etc. Such cases have been designated vegetative neuroses or Basedow types. No true disease is present, but they are on the borderline of normal. For the most part, no true hyperthyroidism eventuates. These people rather preserve their individual peculiarities throughout their lives.

In the moderately severe cases, one has a choice between operation with a short period of pre-operative preparation with iodine and roentgen-ray treatment with prolonged iodine administration. Operation is followed by a more rapid and certain effect. Radiation is less dangerous; its effect is definitely slower and not so certain. Therefore, one may decide in accordance with the courage and economic circumstances of the individual. We strongly advise operation only in acute hyperthyroidism of only a few weeks or months duration, since the outlook here is especially favorable. In older and more severe cases, we are inclined, on the other hand, to try radiation first. Then, if operation is here resorted to, it is often desirable to give iodine not only during the short pre-operative period, but also intermittently over a longer period of time, together with all other symptomatic measures that can be used in order to improve the general condition.

If, however, conservative treatment results in no cure after a few months, we unconditionally advise operation. Temporizing in a half-cured

case of hyperthyroidism always carries with it the danger of the occurrence of thyrotoxic crises.

These crises may arise at any time, their cause being unknown; often they are inaugurated by infection, particularly by pneumonia, to which these hyperthyroid patients are apparently particularly susceptible. A sudden increase in the pulse rate occurs, marked excitation, high fever and general collapse. When this stage has been reached, operation is of no avail. It would be foolish to consider radiation. Many times the patient may be brought out of the crisis by means of iodine, but, for the most part, it ends fatally.

Summary

A review of the non-operative treatment of hyperthyroidism is presented —physical, psychic, dietetic treatment and especially the effect of iodine and roentgen-radiation. Their limits and indications are discussed.

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AN ARTICLE CONTRIBUTED TO AN ANNIVERSARY VOLUME IN HONOR OF DOCTOR JOSEPH HERSEY PRATT

THE DIGESTIVE AND ABSORPTIVE FUNCTION OF THE EXTERNAL SECRETION OF THE PANCREAS *

By MILTON B. HANDELSMAN, M.D., *Brooklyn, New York*

THERE are some types of investigations which require many years of work before any considerable progress is made; studies of the digestive function of the external secretion of the pancreas are of such a nature. The difficulty in preparing suitable experimental conditions in animals, the care needed in controlling the many variable factors of each experiment, and the lengthy chemical analyses, require in some instances as long as a year to study a single case. J. H. Pratt has since 1907 almost continuously studied some aspect of this branch of physiology, and in recent years has actively directed the work of younger men including Hjort, Falcon-Lesses, Herschenson, Rosenblum, Krakower, Golden, Handelsman, Magendantz and others. The number of publications has been few because of the reasons mentioned, but a vast amount of unpublished data has been collected over the years. Some of these studies will be mentioned here.

In general, studies concerning the effect of excluding pancreatic juice from the intestine have given conflicting results. We have had cycles of beliefs varying from the idea that digestion and absorption of fat and nitrogen may be normal, to the belief that no fat and little protein is utilized in the absence of pancreatic juice. A historical survey shows that these conflicts date from early times.

HISTORICAL

As far back as 1682, Conrad L. Brunner [1] removed a large portion of the pancreas of dogs and claimed that the health and digestion of the animals were unaffected. It was Claude Bernard [2] in 1856 who showed that shutting off the pancreatic juice by injecting oil into the ducts caused serious disturbances in the absorption of fat.

Practically all the workers after Bernard were unable to confirm his observations. Frerichs [3] in 1858 tried to destroy the pancreas by numerous ligatures and fed the animals with fat diets; at postmortem examination the lacteals were found more or less filled with white chyle. Herbst [4] in 1853 had the same results. Weinmann [5] in 1853 created pancreatic fistulae in dogs and fed them food rich in fats; he found no fat in the stools. Bérard and Colin [6] extirpated the pancreas in five dogs and left only that

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portion lying next to the portal fissure. The animals lived eight months showing no digestive changes. Bidder and Schmidt [7] in Germany also doubted the results of Bernard. Schiff [8] in 1862 injected paraffin into the main excretory duct in dogs and found that fat digestion went on normally. Martinotti [9] in 1882 asserted that after complete extirpation of the pancreas, no disturbances resulted either in the general condition or in the digestive functions.

The monumental work of von Mering and Minkowski [10] in 1889 in Naunyn's Clinic which cleared up the relation of the pancreas to sugar metabolism, overshadowed the studies in the same clinic regarding the digestive function of the pancreas which were delegated to Abelmann [11] (1890), then a student. Abelmann showed that the removal of the pancreas is followed by enormous losses of fat and nitrogen in the stools. When given in the form of meat or lard, almost all the ingested fat was recovered in the stools whereas when the fat was in the form of a natural emulsion, namely as milk, only about one-half was found in the feces. With partial depancreatization, a larger amount was absorbed. De Dominicis [12] reached the same conclusion. Sandmeyer [13] (1895) reported a partially depancreatized dog whose stools showed a greater amount of fat than had been fed.

That the presence of the pancreas in the body was necessary for digestion and absorption was then generally conceded, but that this action was due to the external secretion of the pancreas was denied. Lombroso [14] (1894) found no disturbance in fat absorption when the pancreatic ducts were tied. Rosenberg [15] (1898) found that in dogs where the pancreas had been separated from the intestine, there was only slight diminution in the absorption of nitrogen, and the fat absorption after having been normal for two months post-operatively was also very slightly diminished. Zunz and Mayer [16] (1906) as well saw no digestive changes. Lombroso [17] (1906) again repeated his earlier work and confirmed his former findings. Burkhardt [18] (1908) obtained results contrary to the results of the above workers. He found the absorption of foods to be diminished when the external secretion of the pancreas was not allowed to enter the intestine—but when the same dog was allowed to lick the secretion from a pancreatic fistula good absorption occurred. To clear up the dispute, Lombroso [19] (1908) went to Greifswald where Burkhardt [18] had done his work, repeated the experiments in the same laboratory in Minkowski's clinic and apparently demonstrated that with the pancreatic juice excluded completely, absorption was good. Fleckseder [20] (1908), Niemann [21] (1909) and Brugsch [22] (1909) were also unanimous in their conviction that normal digestion and absorption could take place when the pancreatic ducts were tied and no secretion entered the intestine. This latter view was generally accepted and was incorporated by Adolph Schmidt [23] (1906) in Von Noorden's "Pathologie des Stoffwechsels."

Many of the above experiments were of dubious value, because the

stools were collected over one day periods which has been shown to be unreliable. However, to explain the above contradictions, three different theories were offered. First Lombroso [19] postulated a pancreatic internal secretion which by its absence did not allow absorption of food when the pancreas was extirpated, but allowed normal absorption even when the pancreatic juice was excluded from the intestinal canal. Secondly, Abelmann [11] (1890), Rosenberg [15] (1898) and Burkhardt [18] (1908) believed that when the pancreatic ducts were ligated, the digestive ferments enter the blood stream and then are secondarily secreted by other digestive glands, thus entering the intestine by other routes.

The third explanation was that most of the earlier workers had actually failed to exclude the pancreatic juice from the duodenum, and that this accounted for the excellent absorption reported in the absence of pancreatic juice. Hess [24] (1907, 1908) after careful anatomical and pathological studies found that there were in many cases three and sometimes four pancreatic ducts in dogs, and that in eight experiments he succeeded only twice in ligating all the ducts. In one of these two instances, only 4.73 per cent of the ingested fat and 54.68 per cent of the nitrogen was absorbed. The other instance showed 48.4 per cent of the fat and 42 per cent of the nitrogen was utilized. This latter result must be accepted with reserve because the dog had double empyema and enteritis. Sinn [25] (1907) corroborated Hess' anatomical studies. Pratt, Lamson and Marks [26] (1909) further pointed out that even after all the ducts are tied, sinuses may form through the necrotic tissue with the result that pancreatic juice again enters the intestine.

More Recent Experimental Evidence of the Rôle of the Pancreatic External Secretion in Digestion and Absorption

It was these investigators, Pratt, Lamson and Marks [26] (1909), who first conclusively demonstrated that the confusion of results was due to most of the workers' failure to exclude pancreatic juice from the intestine. Four out of five dogs were successfully operated upon and proved at autopsy to have had all their pancreatic ducts completely ligated so that none of the digestive ferments could have entered the intestine. These animals showed a markedly diminished absorption of fat and nitrogen as evidenced by the enormous quantities found in the stools both by clinical tests and careful chemical analyses. Similar metabolism and absorption experiments on three additional dogs by Francis G. Benedict and Pratt [27] (1913) yielded the same results. Vinsentini [28] (1914) brought forth more experimental evidence in five dogs with completely ligated ducts also showing that there was a marked decrease in fat utilization. Brugsch [29] (1919) published a report of work done from 1912 to 1915. He was able to ligate the pancreatic ducts and to exclude completely the pancreatic juice in only three out of eight attempts. Those animals successfully operated upon showed a marked diminution of nitrogen and fat absorption leading Brugsch to change his former views and to agree with Pratt.

It must be pointed out in this connection that despite the above experimental results Lombroso [30] (1931) again reaffirmed his beliefs that an internal secretion of the pancreas controls fat absorption. Umber [31] (1926) and Lesser [32] (1925) writing in recent German "Handbücher" still put considerable credence in Lombroso's theory. However, McClure, Vincent and Pratt [33] (1917) showed by direct experimentation that "the absorption of food was no less when the pancreas of a dog was entirely removed from the body than when the pancreas was left in the body but its secretion excluded from the intestines." Vinsentini [28] (1914) obtained only slightly better absorption of fats in dogs with the pancreatic ducts ligated than in those from which the pancreas had been removed. Licht and Wagner [34] (1927) and Falcon-Lesses and Herschenson [35] (1931) conclusively demonstrated that the absorption of foods was the same in dogs in which first only the pancreatic secretion was blocked and then later the pancreatic remainder removed. These studies would tend to discredit completely Lombroso's theory of an internal secretion.

TABLE I

Results obtained by various workers regarding the percentage of dietary nitrogen and fat absorbed in dogs when the external secretion of the pancreas was unquestionably excluded from the intestines

Author	% Nitrogen Absorbed	% Fat Absorbed
Pratt (1907)—ducts ligated	22.2–61.7	4.8–76.6
Vinsentini (1914)—ducts ligated	——	28.7–44.0
Vinsentini (1914)—after pancreatectomy	——	8.7–25.7
Cruikshank (1915)—one stage pancreatectomy	78	32.6
Cruikshank (1915)—two stage pancreatectomy	79.6	72.12
Brugsch (1919)—ducts ligated	21.8–33.5	0–21.8
Licht and Wagner (1927)—ducts ligated and after pancreatectomy	55	0
Pratt, Falcon-Lesses and Herschenson (1931)—ducts ligated	85.3	93.6
Pratt, Falcon-Lesses and Herschenson after pancreatectomy	56.2	95.2
Pratt (1934) with Handelsman and Golden—ducts ligated	47–60	41.5–93.7
Selle (1937)—after pancreatectomy	——	average 89.51
Greenberg (1933) in cats—ducts ligated	51.2–66.8	0–28

Greenberg (1933)[91] employing *cats* obtained results similar to those of Brugsch and Licht and Wagner. He also obtained more fat excreted in the stools than fed.

Although it is now agreed by most experimenters that the exclusion of the external secretion of the pancreas interferes with the digestion and absorption of fats and proteins, there still is tremendous difference of opinion as to how great a rôle it is that the pancreas actually plays. Particularly regarding fat absorption has there been great disagreement, some workers reporting no absorption and others obtaining normal values. We have tabulated the results obtained by various workers in table 1.

It can be seen that Brugsch [29] (1919) and Licht and Wagner [34] (1927) report no fat at all absorbed while Falcon-Lesses and Herschenson [35] (1931)

obtained almost normal absorption. It must be pointed out, however, that Licht and Wagner give no experimental data and a perusal of Brugsch's report reveals that he did not analyze his diets but based his calculations on the amount of solid fat added to the food. If the lipoid content of the meat fed were also taken into account, the percentage of fat absorption in Brugsch's animals would probably be greater.

Cruikshank [36] (1915) first pointed out the importance of the general well being of the animal when absorptive studies are made. Working in Starling's laboratory he showed that a dog which had been carefully depancreatized in a two stage operation absorbed a large percentage of fat, whereas a dog which had been completely depancreatized in one operation absorbed a much smaller amount. Pratt with Falcon-Lesses and Herschenson [35] (1931), giving particular attention to the dogs—a carefully regulated diet which was given in frequent small feedings and included vitamins, as well as plenty of sunshine, exercise, etc.—found that practically normal absorption took place at times in both depancreatized dogs and animals with their ducts ligated without the addition of pancreas in the diet. These animals, however, showed a labile digestive ability and at other times passed the typical large, bulky "pancreatic" stool.

In a further attempt to analyze this situation Pratt directed Handelsman and Golden [37] (1934) to study three dogs with their pancreatic ducts ligated to observe the effect of varying the food components and of varying the quantity of food ingested on the absorptive ability of the animals. No definite relation to the type of food ingested was found. Large quantities of food when given were absorbed in the absolute sense but showed a relatively greater amount excreted in the feces. Furthermore, the animals could not tolerate very large diets for longer than two weeks before an enteritis occurred which responded to treatment when smaller diets were given. They were led to conclude that factors which are as yet unknown influence absorption since not only did the same dog respond differently to the same diet, but different dogs under the same experimental conditions responded in an irregular fashion. The exact rôle of the vitamins added to the diet, a factor neglected by the earlier workers, is not known. Nasset, Pierce and Murlin [38] (1931) showed that there is no effect of yeast on the amount of nitrogen excreted through the feces in depancreatized dogs. The work of Mottram, Cramer and Drew [39] (1922) showing by histological studies that vitamins hasten fat absorption, has not as yet been studied in animals without pancreatic juice. However, both Pratt and Ivy [40] have been impressed with the marked importance of vitamins in their experiments particularly in maintaining the animals in good health and with good fat absorption.

The Length of Life of Animals without External Pancreatic Secretion

Experimenters working with depancreatized dogs reported that these animals died of inanition although they ate large amounts of food and their glycosuria was controlled by insulin. This group of workers did not chemically analyze the stools and reported "tremendous amounts" of fat in the stools microscopically. Since quite early it was found that life could be prolonged in these animals by including raw pancreas in the diet, it was assumed that enzymatic action was the beneficial factor. In 1924 Fischer [41] and Allen, Bowie, McLeod and Robinson [42] pointed out the importance of fatty infiltration of the liver in these animals as a cause of death. Further studies by Hershey and Soskin [43] (1932) and Best [44] (1934) and his co-workers have revealed that lecithin and choline as well as the feeding of raw pancreas can prevent this. The literature on this subject has recently been reviewed by Greene, Handelsman and Babey [45] (1937).

Berg and Zucker [46] reported fatty infiltration of the liver following pancreatic fistulae. A perusal of many autopsy records of dogs with ligated pancreatic ducts studied by J. H. Pratt (unpublished) reveals no case with evidence of abnormal infiltration of the liver with fat. This coincides with the experience of Von Prohaska, Dragstedt and Harms [47] (1936) who also find no relationship between the deprivation of the external secretion of the pancreas and fatty livers. Bloom and Handelsman [48] reported a case of a young dog with naturally occurring diabetes which died because of fatty changes in the liver (jaundice, etc.). The acinar tissue was for the most part well preserved and stool studies revealed no evidences of pancreatic secretion deficiency, but practically no islets of Langerhans were found. An internal secretion of the pancreas which prevents the occurrence of fatty livers has actually been isolated by Dragstedt, Von Prohaska and Harms.[49]

Absence of the external secretion of the pancreas from the intestine does not seem incompatible with a fairly long and healthy life. Several of J. H. Pratt's dogs with ligated ducts lived for long periods of time. "Zep" lived for over three years and "Nellie" over 2½ years without ever being fed pancreas or enzymatic preparations.

Complete pancreatic fistulae with continuous loss of the secretion outside the body leads to death in five to eight days. The mechanism leading to the fatal ending in these cases has been studied by Elman and McCaughan [50] and others,[51] and has been found not to be related to the digestive function of the pancreatic secretion but to the acid-base economy of the animal. Large quantities of physiological saline administered to such dogs can prolong their lives for a longer period of time.

The Digestion and Absorption of Fats in the Absence of Pancreatic Juice

The pancreas played the rôle of "star witness" in the earlier arguments of the physiologists as regards the necessity of the splitting of fats before

absorption. However, fat recovered in the stools is for the most part well split even when the greatest source of lipase, the pancreatic juice, is absent from the intestine. This fact was first noted in the first animal experimentations of Abelmann [11] in 1890 where depancreatized dogs were used. Pratt, Lamson and Marks [26] (1909) also found excellent hydrolysis of the fats in the stools of animals whose pancreases were allowed to remain in the body with the pancreatic ducts blocked; for example, one of the dogs studied excreted 88.7 per cent of the ingested fat in his stools and 70 per cent was in the form of fatty acids and soaps. H. Wendt [52] in his review has collected the clinical literature on this subject with the same conclusions.

The factors involved in the mechanism of this excellent fat splitting in the absence of pancreatic juice have been puzzling. Three other sources of lipolytic activity have been known to exist. Volhard [53] clearly established the presence of a fat hydrolyzing enzyme in the stomach which is active in acid medium, and Boldyreff [54] (1905) demonstrated an enzyme of similar nature in the intestine. It has been known that many bacteria also have the power to split fats particularly in the colon.

Umber and Brugsch [55] (1906) interesting themselves in this problem first suggested that the gastric lipase might play a rôle when there was a deficiency or absence of pancreatic juice. They reported a single observation: on sacrificing a depancreatized dog, the fat collected between the pylorus and papilla was only 18.2 per cent split whereas that in the lower ileum was 42 per cent split. This made them minimize the importance of the gastric lipase and led to search for lipase in other organs.

Gross [56] (1912) in studying two cases where atrophy of the pancreas was clinically diagnosed (one case later proved at autopsy) searched for a cause of the excellent splitting of fats in these cases. He found in these patients that gastric juice when left with neutral fat in an incubator at 38° for an indefinite length of time split the fats. Since this did not occur when toluol or chloroform was added, he supposed that bacterial action in the stomach and upper intestine caused these results.

Nothmann and Wendt [57] in 1931 criticizing Gross' results instituted experiments on five depancreatized dogs to which they fed olive oil test diets. The dogs were killed from four to eleven hours after having been given the test diets and the fats in the small intestine were analyzed quantitatively and for the amounts hydrolyzed. They found only 2.01 per cent to 3.98 per cent of the fats in the small intestine split whereas in the large bowel 14.82 to 22.11 per cent were in the form of fatty acids and soaps. This led them to emphasize the lipolytic activity of the bacteria in the colon. In two of their experiments wherein the total fats remaining in the intestinal canal were determined, they were able to recover 89 per cent of the ingested fat in one case and almost 100 per cent in the other. The amount of fat absorbed as well as the poor splitting stands in contrast to the experiments where excellent absorption of fats has been found when balanced diets are

fed to the animals. We have tabulated from reports in the literature the results of analyses of intestinal contents of dogs killed after a normal meal and have included some unpublished results obtained by J. H. Pratt (table 2).

TABLE II

% Split in	Normal Dogs			Depancreatized Dogs		Dogs with Pancreatic Ducts Ligated
	Starling and Pincussen	Abelmann	Umber and Brugsch	Umber and Brugsch	Pratt (unpubl.)	"Toby" Pratt, Golden and Handelsman (unpubl.)
Stomach	30–40%	—	—	—	—	31.3%
Duodenum	—	—	30.2%	18.2%	—	32.3%
Jejunum	—	32%	—	—	41.5%	—
Ileum	—	57%	48.9%	42.0%	46.4%	31.9%
Colon	—	76%	81.0%	72.9%	—	45.0%
Stools (same diet)	—	—	—	—	—	51–55%

A careful analysis of the factors that contribute to these opposite results obtained with olive oil administration in contrast to balanced diets revealed interesting results. Nothmann and Wendt [58] found that after iodipin and egg yolk mixtures, roentgen-ray studies in depancreatized dogs showed enormously rapid gastric emptying time. They checked this observation with quantitative chemical analyses of the gastrointestinal contents of depancreatized dogs killed at various intervals after being fed olive oil test meals. Independently, Beguria working in the Tufts College Physiology Laboratory with olive oil-barium sulfate mixtures obtained similar results in roentgen-ray studies of depancreatized dogs; in some dogs, the olive oil mixture was in the ileum in one hour with complete emptying of the stomach by that time.

Unpublished roentgen-ray studies by Pratt done in 1917 revealed only very slight changes in the gastrointestinal motility of several depancreatized dogs and animals with their pancreatic ducts tied. These studies were done with plain barium sulfate suspensions or with ordinary canine diets mixed with barium. This was substantiated by other methods. In practically none of our dogs did carmine appear in the stools before 15 hours, usually 24 hours. Furthermore on sacrificing one dog four hours after a meal 58 per cent of the food was still in the stomach and only 11 per cent was in the proximal colon. Yesko [59] and Fauley and Ivy [60] found a slightly decreased gastric emptying time in such dogs; the latter attribute this as due to a normal hunger mechanism.

Dr. Beguria was kind enough to do gastrointestinal series on two of our dogs with ligated pancreatic ducts. With ordinary barium sulfate suspension in water, a practically normal motility was found, but with the olive

oil-barium sulfate mixture, an extremely rapid gastrointestinal motility was demonstrated. This latter result stands in contrast with the work of Nothmann and Wendt [58] who did not find the rapid passage of the olive oil in dogs with ligated pancreatic ducts but only in depancreatized dogs. Because of their findings, they proposed the theory that an internal secretion of the pancreas regulates gastrointestinal motility. The studies of Pratt and Beguria do not offer warrant for such a theory.

The unusual acceleration of the passage of olive oil and iodipin through the intestines, a condition which does not occur with usual diets in the absence of pancreatic juice, explains the extreme differences in digestion and absorption found by Nothmann and Wendt [57] and other workers. This specific " diarrhea " of the oils does not allow sufficient time for their splitting and absorption. This difficulty does not exist with other foods.

The problem of how the fats of usual diets are split in the absence of pancreatic lipase cannot be explained entirely by slow intestinal motility. A perusal of table 2 reveals that a considerable amount of fat is already split in the stomach (25 to 30 per cent) in both normal and depancreatized dogs. Careful control studies by Pratt and Golden (unpublished) revealed that the diets of dogs in the Tufts laboratory were in some instances already 10 to 15 per cent split before ingestion. This was traced to the use of cans of Klim opened for a time before use. In other unpublished experiments, the gastric contents of two dogs with ligated pancreatic ducts were analyzed four hours after feeding and yielded 23.5 per cent to 27.2 per cent of the fats in the split form. Although this is minimal when compared to the 40 to 50 per cent splitting usually found in the ileum, the gastric lipase may really be of some significance. Pratt, Golden and Handelsman (unpublished) studied the pH of the intestinal contents of dogs without pancreatic juice who were killed four hours after a meal. The hydrogen-ion concentration showed strong acidity throughout. The studies of Hoerner[62] showed that normally the pH of the duodenal content may range from 7.81 to as low as 3.31. In dogs without pancreatic secretion, although the range found was within these limits, the lower hydrogen-ion values were most often found. Since the gastric lipase hydrolyzes fats optimally in an acid medium, its action may possibly be carried on in the lower intestinal canal in the absence of pancreatic juice.

Minkowski [63] (1890) expressed the belief that an intestinal lipase hydrolyzes the fat. However, the importance of intestinal lipase is minimized by Hull and Keeton [64] who find the concentration of gastric lipase five times greater. Also Koskowski and Ivy [65] (1926) found no change in the *succus entericus* in the absence of pancreatic juice and Fauley and Ivy [60] found a hypersecretion of gastric juice under those conditions.

The other locus of lipolytic activity, the colon, does not seem to be important regarding fat absorption. Nakashima [66] (1914) and Verzár [67] (1937) have found no evidence of the ability of the colon to absorb fat although Yamakawa [68] (1929) claims this to be possible.

Studies of fat absorption approached from other angles have clarified the rôle that fat splitting actually plays in the resorption of fat. Pflüger [69] (1901) had advanced the "saponification theory of absorption" and insisted that there must be complete splitting of fats before absorption could take place. On the other hand Mellanby [70] (1928), minimizing the importance of fat hydrolysis, showed that the amount of lipase in the pancreatic juice of a cat is so small that it could merely serve as a mechanism to initiate emulsification of the ingested fat by providing only a very small amount of soap. F. Verzár (1936) has reviewed the literature on this subject as well as his own works which have clearly demonstrated the importance of lipase and bile in fat absorption. He showed that neither fine emulsions of a neutral fat, nor neutral fat together with lipase, nor neutral fat emulsified with bile acids were absorbed from the intestines of dogs whose bile ducts were tied. But when neutral fats were put into the intestines along with lipase and bile acids, 74 per cent were absorbed after 24 hours. The bile acids do not act upon neutral fats, but they form physical complexes with fatty acids resulting in combinations which are more soluble and diffusible than either of the parent components and which are easily absorbed. These results have been confirmed by Riegel, Elsom and Ravdin.[71]

From these studies it can be seen why good fat absorption may take place in the absence of pancreatic juice as long as some lipolytic agent initiates the hydrolysis of neutral fats. The finding that an animal without pancreatic secretion entering the intestines may show good absorption at one time and poor at another time indicates that other factors as yet unknown must play a great rôle. Further studies must clarify the importance of vitamins, mineral content, the differences of various fats, etc.

Since the fatty acid-bile acid complexes described by Verzár [67] are broken down in a medium with a pH below 6, and since the pH of the intestinal canal of a dog without pancreatic juice can be as low as 3.5, another factor suggests itself for study. One would suspect that the administration of alkalies might aid fat absorption, but experiments by Poczka and Fischel [72] on a patient with pancreatic insufficiency showed that such treatment actually increased fat excretion.

Experimental studies involving the administration of pancreas (fresh or extracts) to animals without pancreatic secretion have been contradictory and give no conclusive proof of the rôle played by pancreatic lipase. The consistent improvement obtained in the digestion of proteins and carbohydrates in such substitution experiments does not seem to hold for fat. Pratt, Lamson and Marks [26] believed they obtained better fat absorption after the administration of pancreatic extract. Nothmann [80] found marked improvement in fat absorption in depancreatized dogs when large doses of "pankrophorin" were given. Absorption studies in a patient with achylia pancreatica by Poczka and Fischel [72] revealed that the majority of proprietary preparations in Germany with the exception of "Pancreatin-dispert," did not

prevent fat loss in the stools. Very recent experiments with depancreatized dogs by Selle [81] using enteric coated as well as plain pancreatic extracts (potent in vitro) showed no improvement in fat absorption, although in the same experiments the nitrogen utilization was markedly increased. However, Selle who reported no benefit, had excellent (90 per cent) fat absorption even without the administration of pancreatic enzymes whereas Nothmann and Wendt who were impressed with the efficacy of oral pancreatin in depancreatized dogs had had previously only 4.3 per cent of the dietary fat absorbed. Similarly Sarzana [82] who obtained only 50 per cent absorption of olive oil in pigeons with ligated pancreatic ducts, also noted improvement up to 84 per cent absorption when pancreatic juice was given along with the fat. These differences in reports of success in pancreas administration point again to the numerous complicating factors controlling fat absorption.

The Nature of the Fat in the Feces of Animals with Pancreatic Steatorrhea

Bloor, Sperry and their co-workers [73] have shown the lack of relationship between dietary fat and the fat excreted in the stools of normal animals. A. Krakower [74] has shown this to occur also in humans. In normals, after all the dietary fats are absorbed, apparently fat is again excreted by the intestines to form the fecal lipoids which are entirely independent of the food ingested.

Studies in Pratt's laboratory by Krakower and Rosenblum (unpublished) revealed a close similarity of the fat in the stools of animals deprived of pancreatic juice to the dietary fat. When fed olive oil, the iodine number of the fecal fat approached that of olive oil; when butter was fed, the iodine number of the fecal fat approached that of butter.

The external pancreatic juice has been found by Tangl and Berend [75] (1930) and Tangl [76] (1932) to contain a "dehydrogenase" which is activated by bile. Berend [77] (1933) demonstrated such an active enzyme in the pancreas alone and Quagliariello [78] isolated a desaturating enzyme in bile alone. Artom [79] has reviewed experiments by Italian workers demonstrating similar desaturization of fats by many tissues and even by *B. coli*. On the other hand, there is evidence that unsaturated fats may be preferentially absorbed. Apparently these factors did not influence the fats studied by Krakower and Rosenblum in the above experiments with dogs whose ducts were ligated. In other experiments where Nucoa was employed instead of butter or olive oil, the close similarity between ingested and excreted fats was not obtained, the latter being more unsaturated. It is possible that this difference was due to the presence of desaturating enzymes in the intestinal canal.

The Digestion and Absorption of Carbohydrates in the Absence of Pancreatic Juice

Clinically it was maintained by F. Mueller that the digestion of starches was not necessarily impaired in the absence of pancreatic secretion. Furthermore, studies on "intestinal catarrh" and cases with increased gastrointestinal motility due to causes other than pancreatic disease have shown large amounts of carbohydrates in the stools. Thus the presence of starch in the stools has been more or less neglected by the clinicians as a comparatively insignificant factor in the absence of pancreatic enzymes in the intestine.

Rosenberg [15] in 1896 pointed out the presence of starch in the stools in these cases. It is only recently that this problem has been studied experimentally. Dogs lend themselves well to this study since their saliva contains no ptyalin. Hjort [35] working in Pratt's laboratory studied normal dogs on a comparatively large diet of ground meat, cracker meal, butter and vitamins and found the stools to contain only 1.08 per cent starch (analyzed as sugar); the same animal after the pancreas had been completely separated from the intestine passed stools containing 14.23 per cent starch (as sugar). Handelsman, Golden and Pratt (unpublished data) found the stools of two dogs with similar operative interference to consist of 0 per cent to 9.1 per cent carbohydrate (analyzed as sugar) when diets low in carbohydrates were fed; and to contain 21.5 per cent to 46.6 per cent sugar when high carbohydrate diets were fed. Beazell, Schmidt and Ivy [83] fed dogs with the pancreas separated from the intestine with diets containing 62 per cent starch, and they found that 18 per cent to 39 per cent of the stools consisted of starch. Sekikawa [84] found that feces of normal animals contain 80 to 190 mg. carbohydrate per gram of stool; after ligation of the pancreatic ducts the carbohydrate concentration of the stools rose to 190 to 230 mg. per gram of stool while after pancreatic fistula the concentration was still higher, 240 to 500 mg. per gram of stool.

Studies of the percentage of starches in the stools do not give a true picture of the amount actually absorbed. A good example of this occurred in the dog "Nellie" where Pratt and his co-workers found after a high carbohydrate meal absorption of 92.6 per cent of the ingested cracker meal, yet stool analysis showed 30.1 per cent of the feces to consist of carbohydrate. For the most part, carbohydrates seem to be more than 90 per cent absorbed, when the intake is not too excessive even in the absence of pancreatic juice and this good absorption seems to be independent of the relative fat and protein content of the diet.

To explain this good absorption, recently Zucker, Newburger and Berg [85] (1932) again renewed the theory of Rosenberg [15] that the pancreatic enzymes may be secreted by other organs. These workers studied the increased serum and urinary amylase in dogs whose pancreatic ducts were blocked and were impressed with the fact that the disappearance of the in-

creased serum amylase is not accounted for by its excretion in the urine. They report evidence of increased amylotic activity of the bile in cases where the pancreatic ducts have been tied. This was first demonstrated in birds by Langendorff [86] in 1879. This type of compensatory mechanism was also studied by Schegalow [87] in 1902 who reported increased proteolytic activity in the bile after ligating the pancreatic ducts and Lombroso [17] (1906) who found the same for lipase. Pflüger [89] (1905) expressed his approval of this theory. However, the excellent absorption of carbohydrates reported by Pratt [35] in dogs with the pancreas removed from the body does not allow much importance to be attached to this theory.

Beazell, Schmidt and Ivy [83] found that administration of pancreatin as well as other diastase preparations markedly decreased the amount of carbohydrate in the stool of dogs with their pancreas completely disconnected from the intestine. Such excellent therapeutic results would tend to substantiate the impression that it is actually the absence of diastatic digestion in depancreatized dogs that leads to the excretion of carbohydrates in the stools rather than other causes such as rapid gastrointestinal motility, improper pH of the intestine or interference with the absorptive processes.

That the compensatory mechanism of carbohydrate digestion can be strained in some cases by the excessive administration of starchy foods was shown by one of Pratt's dogs.[35] This animal was unsuccessfully operated upon and not all the pancreatic ducts were ligated as was proved at autopsy and also noted clinically by the absence of the typical "pancreatic stools." Whereas fat and nitrogen were normally absorbed, large quantities of starch appeared in the stools. Apparently in this case of hypochylia pancreatica, the amount of pancreatic juice was insufficient for the complete digestion of carbohydrates.

The Digestion and Absorption of Nitrogenous Foods in the Absence of Pancreatic Juice

In normal animals, the amount of fecal nitrogen does not vary with changes in the amount of ingested nitrogen, and even remains the same on a protein-free diet. The fecal nitrogen may be increased by raising the indigestible, non-nitrogenous bulk of the diet while changes in the digestible food components have practically no effect.[90] It would seem that the fecal nitrogen originates in a manner similar to that of fecal fat, namely as a secretion product of the bowel rather than being a true indigestible residue.

In dogs without pancreatic juice entering in the intestine, usually 35 per cent to 55 per cent of the ingested nitrogen is excreted in the stools. Similar results have been obtained in cats by Greenberg [91] who found 33.2 per cent to 48.8 per cent excreted. Occasionally higher values are obtained (see table 2). That this increased fecal nitrogen represents the undigested food nitrogen has been recognized by clinicians by tests with cell nuclei and striated meat fibers found in the stools after the ingestion of meat. Detailed

chemical studies of the type of nitrogen found in the stool of depancreatized animals have not been made probably because of the difficulty in controlling gastrointestinal motility as well as bacterial putrefaction in the colon. (Review by Pratt.[92]) There is also a lack of data concerning the intermediary protein breakdown products in the intestine in the absence of tryptic digestion, a phase in which the gastrointestinal allergists are now interested.

F. G. Benedict and Pratt [27] studied the specific dynamic action of meat feeding in dogs in which the pancreatic secretion was absent. After the feeding of 500 grams of meat, the 24 hour increment in CO_2 production was 28 per cent for a normal animal, compared to 17 per cent and 22 per cent in experimental animals; after 750 grams of meat the increase in metabolism in a normal dog was 62 per cent as compared with 48 per cent, 43 per cent and 25 per cent in animals without pancreatic secretion. Kúthy [88] by direct experimentation in normal rats has established that the specific dynamic action of proteins parallels their absorption rate. The data of Benedict and Pratt on closer examination reveal that the increased CO_2 production of the experimental animals after meat feeding as determined over four hour periods, approximately parallels that of the control animal with the exception that there was a diminution in the quantity produced. Since the animals were in nitrogen balance, it would seem that protein absorption in animals without pancreatic juice proceeds normally except for the decreased amount of absorption.

The problem of nitrogen balance in depancreatized dogs has been studied by Nasset, Pierce and Murlin [38] who showed that such dogs may have an increased nitrogen retention or normal balance even when large quantities of nitrogen are lost in the stools.

An interesting problem has been brought up by the work of Selle [81] who found that pancreatin administration reduced the weight of the stools of depancreatized dogs by 50 per cent and reduced the fecal nitrogen 35 per cent to 65 per cent. Fat excretion in these animals, 10 per cent to 11.4 per cent, was almost normal, and was uninfluenced by pancreatin administration. Since no carbohydrates were fed to these animals during the metabolism periods, it would seem that the reduced bulk of the stools after pancreatin paralleled the decreased nitrogen excretion. This observation is interesting inasmuch as the bulkiness of the pancreatic stool is one of its typical features. A perusal of the fecal analyses by Handelsman, Golden and Pratt [37] reveals a relationship between increased nitrogen ingestion and the increased dried weight of the stools, but the bulkiness did not seem to depend upon an increase in the percentage of nitrogen in the stool or on the percentage of nitrogen absorbed. The enormity of the "pancreatic stools" has not been completely explained. Incomplete studies in Pratt's laboratory with the diets used would seem to indicate that the dried ash content of the stools is not the cause of the large size of the feces. On calculating the results of many careful dried stool analyses there has been found an "un-

determined residue" when the carbohydrates, fat, ash and proteins (N × 6.25) have been totaled. This undetermined residue is probably greater than calculated since a part of the nitrogen in the stool is not from protein.

Conclusions

Care must be used when studying the literature concerning the external secretion of the pancreas. The earlier studies reported good absorption of food when the pancreas was separated from the intestine and attributed this to an internal secretion of the pancreas regulating absorption. However, these conclusions were based on experiments where the pancreatic juice was not completely excluded from the intestine. After more careful surgical interference the same digestive disturbances were found as after pancreatectomy. Although the early experiments showed rather poor absorption of foods, in later studies employing smaller feedings, including vitamins, and giving more care to the general well-being of the animal, fairly good absorption of foods occurred. In contradiction to the good absorption of the unsuccessfully operated dogs, the animals actually without pancreatic secretion in the intestine show a labile digestive mechanism good at times and poor at other times. Only in the carbohydrate fraction does this lability seem to depend on the diet as manifested by a higher percentage of carbohydrate in the stools. The nitrogen and fat absorption are also labile, but the factors causing these variations are not completely understood. Fat digestion and absorption are particularly complicated. The duty of the pancreatic juice seems to be to split the neutral fats in preparation for the absorption of the fatty acids combined with bile acids. In the absence of the pancreas a compensatory mechanism splits the fats; the gastric lipase may play some rôle in this. The significance of the lowered pH of the intestinal canal in the absence of pancreatic juice as well as a singularly rapid gastrointestinal motility when oils are fed is not as yet known. Most of the digestive and absorptive phenomena found in depancreatized dogs are found in dogs with their pancreatic ducts ligated. The internal secretions postulated to explain fat absorption or to regulate gastrointestinal motility are not substantiated. The fatty infiltration of the liver in depancreatized dogs, however, seems to be related to an internal secretion of the pancreas.

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CASE REPORT

THE SYNDROME OF DYSPHAGIA AND ANEMIA *

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"THERE is a variety of dysphagia, not uncommon in middle-aged women, which in all cases presents almost identical signs and symptoms and which reacts uniformly to treatment, but as to the pathology of which we are ignorant." This statement by Brown Kelly [1] in his original discussion of the subject is still true of the syndrome he described. Kelly [1] and Paterson,[2, 3] in 1919, outlined the symptom complex of "spasmodic dysphagia" as one clearly distinct from that of "globus hystericus," achalasia of the cardia or organic obstructive lesions of the esophagus. Their patients were women, the majority of whom were between 40 and 50 years of age. The outstanding symptom in each patient was either a slowly or a rapidly appearing dysphagia, referred to the level of the larynx, in the absence of any previous chemical or thermal esophageal injury. Several patients related symptoms common to the neuroses. Most of them were undernourished. Both authors found a pallor of the pharyngeal mucous membrane, the tongue surface smooth and devoid of papillae. The mouth corners were fissured, there was notable ptyalism. In several patients an easily ruptured membrane extended transversely across the entrance to the esophagus. In others there were firm, approximated bands in the mucosa forming a closure of the gullet at the site of the complaint. These bands apparently were not on a cicatricial base and yielded readily to pressure from a tube, bougie, or endoscopic instrument. In many instances there seemed to be simply increased muscular tone at the entrance into the esophagus. The patients had no intermittent symptoms or other characters of hysteria. Dilatation maneuvers gave the patients definite relief and Kelly concluded, from a particular study of 10 patients, that the disorder was a spasm of esophageal muscle developing as a result of faulty innervation, probably failure of a proper local reflex arc through the plexuses of Auerbach and Meissner.

Vinson,[4] in association with Plummer, after observations on 69 patients (only 12 were males) was impressed with the occurrence of an anemia of the hypochromic type in dysphagia. The onset of the disease in the majority of his patients was marked by a rather sudden hindrance in swallowing solid food. The symptoms often were tolerated for years before a physician was sought. Roentgenographic and esophagoscopic examination gave no evidence of disease. Twelve of these patients had palpable spleens. The passage of an esophageal sound gave excellent results when followed by Blaud's pills, Fowler's solution and encouragement to eat. Vinson was impressed also by the hysterical manifestations of these patients. Since this report in 1922, the disorder frequently

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has been called the Plummer-Vinson syndrome. Moersch and Connor [5] collected a series of 65 such hysterical dysphagias, all being found in women between the ages of 23 and 63 years.

Hurst [6] reported a case which suggested that infection of the throat, as by streptococci, might give rise to a reflex spasm in the esophagus. Ryle [7] reported a patient having no delay in the passage of barium and in whom he felt hysteria was the etiologic factor. Cameron [8, 15] reported an analysis of 25 case studies. He emphasized the smooth, pale, dry mucous membrane of the mouth and fissures extending from the mouth corners over the skin. All of his patients were women between 41 and 60 years of age. The dysphagia usually was located at the level of the larynx. Splenomegaly was found in eight instances. In 15 patients, the hindrance in deglutition appeared to have preceded the anemia. Cameron considered atrophy of the mucous membrane, with the probable loss thereby of both mucous secreting glands and properly functioning sensory nerve endings, as of great significance in the mechanism of the dysphagia. Jones and Owen,[9] in summarizing the clinical characters of the disorder, were impressed by the long duration (one to eight years, in their experience) of the dysphagia. Evans,[10] considering the disorder not a local disease but a local manifestation of a general disease, presented incomplete evidence that syphilis may have been the causative factor in some instances. He referred to a necropsy on one patient but gave no details as to the microscopic findings in the esophagus. Witts [11] described anemia and dysphagia in 13 women with characteristic findings and excellent response to therapy with iron. The anemia was definitely microcytic in all but one patient.

Suzman,[12] in 1933, reviewed the previously reported cases and added eight from his experience. One of his patients died following perforation of the esophagus by an unguided filiform bougie. In an autopsy on this patient, the sections from the esophagus showed marked desquamation of the superficial epithelium and a few areas of unequivocal keratinization. There was moderate infiltration by lymphocytes and plasma cells. The musculature was atrophied. Of greatest importance was his observation that there were no demonstrable changes in the nerve plexuses. Hoover [13] reported on a series of 17 cases, in seven of which a definite band or web was found in the upper end of the esophagus. He observed that the passage of the esophagoscope alone relieved the dysphagia in most instances. McGibbon,[14] from a study of seven such patients, emphasized a characteristic glossitis, stomatitis and atrophic pharyngitis as the essential findings. Splenomegaly, koilonychia, achlorhydria, fissures at the angles of the mouth, brownish discoloration of the skin and increased fragility of the erythrocytes were occasionally associated with the syndrome. Five of his patients had a web or other demonstrable upper esophageal lesion.

Many of the reported histories indicate that dysphagia precedes the onset of anemia but occasionally the reverse is true.[15] Patterson [3] stated that the anemia comes late in the disease and is to be regarded as a secondary manifestation of the dysphagia. Benhamou and Cohen-Solal [16] regarded the entire symptom complex as being secondary to an essential hypochromic anemia.

Proper consideration of dysphagia resulting from a failure of the introitus of the esophagus to receive and adequately transmit solid food and fluids, requires a careful elimination of palpable lesions which may give similar symptomatology. Such recognized causes of obstruction are retropharyngeal ab-

scess, bulbar paralysis, pharyngeal, laryngeal or esophageal neoplasm, congenital malformation, foreign body, cicatricial contraction, pulsion or traction pouch, mediastinal mass, and others carefully listed by Hutchison.[17] Impaired deglutition has been noted in patients with scleroderma, progressive muscular dystrophy,[18] exostoses of margins of cervical vertebrae,[19] and unilateral pulmonary fibrosis.[20]

Since the treatment of this well identified clinical syndrome has been remarkably successful, rarely does an opportunity for postmortem study appear. There have been found but two previously reported autopsies on patients who had the clinical syndrome of idiopathic dysphagia and anemia.[10, 12] The patient in the following case report had no demonstrable cause for dysphagia. The pressure of the thyroid lobes on the esophagus was associated with normal deglutition for too long a time for it to serve as an explanation of dysphagia. The age of the patient when her symptoms appeared and the manner of her death, exsanguination by bleeding from multiple points in the gastrointestinal tract, are unusual.

Case Report

Mrs. E. H., aged 66 years, entered the Davis Memorial Hospital, January 17, 1936, complaining of loss of weight and weakness for the previous six months and of dysphagia for six weeks. The embarrassment in deglutition was slight until January 14. For the few weeks prior to the latter date she observed that both liquid and solid foods were swallowed with some difficulty. Three days before admission her son observed that she seemed to be unable to take any of her food and that saliva drooled from her lips as she attempted to swallow. She left the table in the middle of the meal and took little or no nourishment during the next two days. She complained of no fatigue in mastication. There was a known loss of 30 pounds in weight in the six months prior to her hospital admission.

The patient had been in apparent good health previously, save for a few aching pains, of the type associated with hypertrophic arthritis, in the lower back and thighs since the age of 60 years. The menses ceased at the age of 40 years. Her mother died at the age of 58 years with a clinical diagnosis of carcinoma of the stomach.

The patient was cachectic, weighing but 81 pounds, and could scarcely walk from weakness. Her skin was generally atrophic and loosely attached to the body. Several fissure-like wrinkles radiated from each corner of her mouth. A nodular but fairly symmetrical enlargement of both lobes of the thyroid was noted. One pea-sized, moveable lymph node was palpable in the right supraclavicular fossa. All upper teeth had been removed, a few worn teeth remained in the lower jaw. The buccal mucous membranes were dry, the tongue surface was notably smooth as in atrophy of the lingual papillae. There was no evidence of paralysis of any of the cranial nerves. The skeletal reflexes were unchanged. The abdomen was scaphoid in contour. The thorax was moderately hyperresonant. The heart sounds were faint; there was a systolic murmur of low intensity and short duration heard over the apex. The blood pressure was 138 systolic and 96 diastolic.

In the presence of the physician, the patient seemed unable to initiate the act of swallowing. At each attempt, after bobbing her head a few minutes, she sought to expectorate soft food and water alike. In the fluoroscopic room, the thick barium mixture accumulated in a peculiar round mass, the size of a golf ball, immediately below the level of the cricoid cartilage. The patient was unable to move the bolus farther and, after being subjected to strong reassurance and persuasion for five minutes, regurgitated the mass. She could not be induced to attempt to swallow the barium again. When an effort was made by one of us (T.M.G.) to pass the eso-

phagoscope the instrument was firmly grasped in the upper esophagus. The view obtained was that of a swollen, hyperemic mucosa filling the end of the esophagoscope in every maneuver and, with the degree of force considered safe, the endoscope could be passed no farther.

The urine contained a trace of albumin. The blood had a hemoglobin value of 56 per cent (Sahli), 3,720,000 erythrocytes per cubic millimeter, and a negative Kahn reaction.

The patient was fed twice daily for four days by gavage through a heavy Ewald aspirator tube. In the first feedings the tube had to be forced through the upper

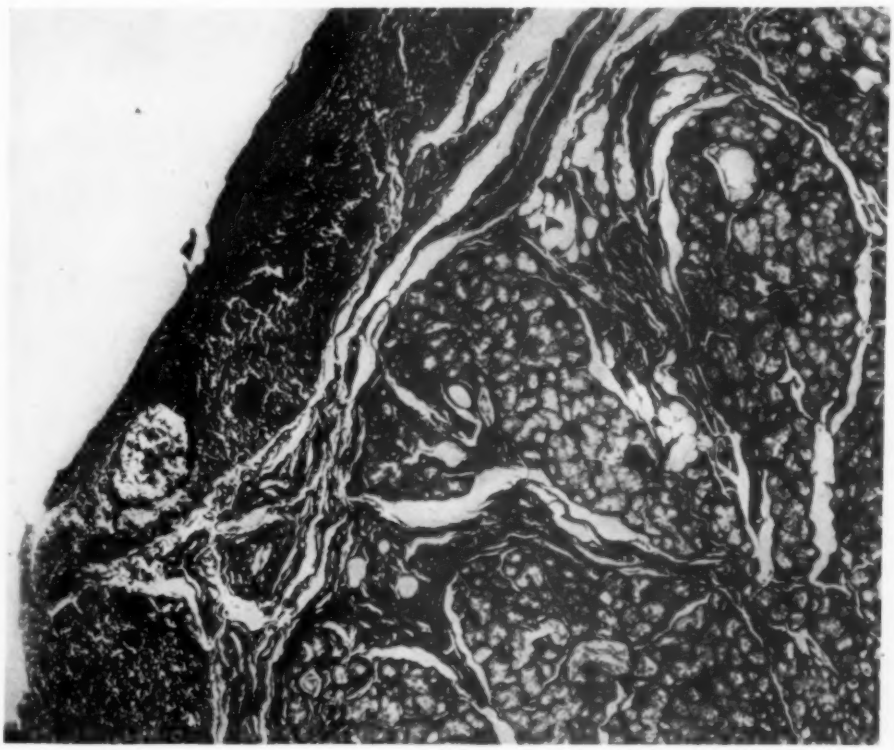

FIG. 1.

esophagus with more than the customary manipulation and pressure. By the third day the Ewald tube could be passed with distinctly less effort. At no time was free hydrochloric acid found (histamine was not used). The patient expectorated large amounts of mucoid saliva, requiring a cup constantly at her bedside. After the fourth day in the hospital she could swallow both soft food and liquids, the former more readily. The patient gained in strength and left the hospital January 25, eight days after admission, with instructions to take seven grains of reduced iron three times each day.

After seeming to improve for four days at home, the patient, on January 29, suddenly became very faint, dizzy, and fell to the floor. She had to be helped to her bed by her daughter. There was no loss of consciousness and no evidence of paresis of any extremity. After an hour in bed, she was well enough to be up and about the bedroom again but she complained of a vague abdominal discomfort.

She was given an enema and returned a tarry, offensive stool. During the night she made, alone, two trips to the bathroom. It is not known whether she defecated. The following morning the patient ate a small breakfast and again complained of marked dizziness and weakness. An hour or so after breakfast, she vomited a moderate amount of dark coffee-ground material which her daughter, a graduate nurse, recognized as blood. The patient made a 15 mile trip by ambulance to the hospital, losing consciousness five minutes before admission. Within an hour she had ceased breathing.

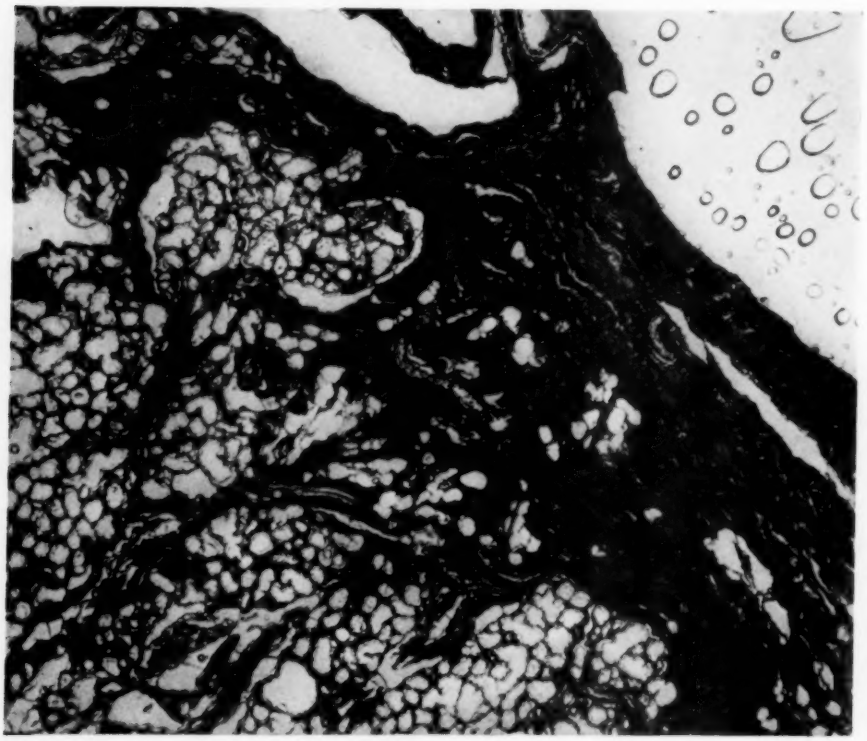

FIG. 2.

A postmortem examination was started 30 minutes after death. There was a minimal quantity of panniculus adiposus. The distended intestinal loops were speckled fairly generally with subserous hemorrhages, 2 to 15 mm. in diameter. The small intestine yielded 500 c.c. of clotted blood and bloody fluid. An equal quantity was found in the stomach. Innumerable bleeding points, not over 2 mm. in diameter, were present in the mucosa of the upper jejunum, duodenum and stomach. No other lesion could be demonstrated in the abdominal viscera save for recent hemorrhages into both adrenal glands. The spleen was small, the liver of average size.

The heart weighed 290 grams. There were a few atheromatous plaques in the proximal aorta. The coronary arteries were patent. The mitral valve leaflets were scarred and fused so as to admit but one finger into the valve. The mitral annulus measured 7.0 cm. in circumference. Other cardiac measurements were normal. The lungs showed no significant alteration.

In the lumen of the esophagus at its lower end was one-half of an insufficiently masticated stewed prune. There was no obstruction at the cardia. The inner surface of the upper half of the esophagus was hyperemic and had numerous irregular areas, 4 to 10 mm. across, which were denuded of mucosa. There was no demonstrable obstruction. The entire esophagus, with the tongue and stomach attached, was removed for examination. The thyroid lobes were each approximately 3 by 3 by 5 cm., extended posteriorly beyond the trachea and left definite imprints upon the lateral surfaces of the collapsed esophagus. The surfaces made by cutting the thyroid revealed small cysts and areas of calcification in the substance of the gland.

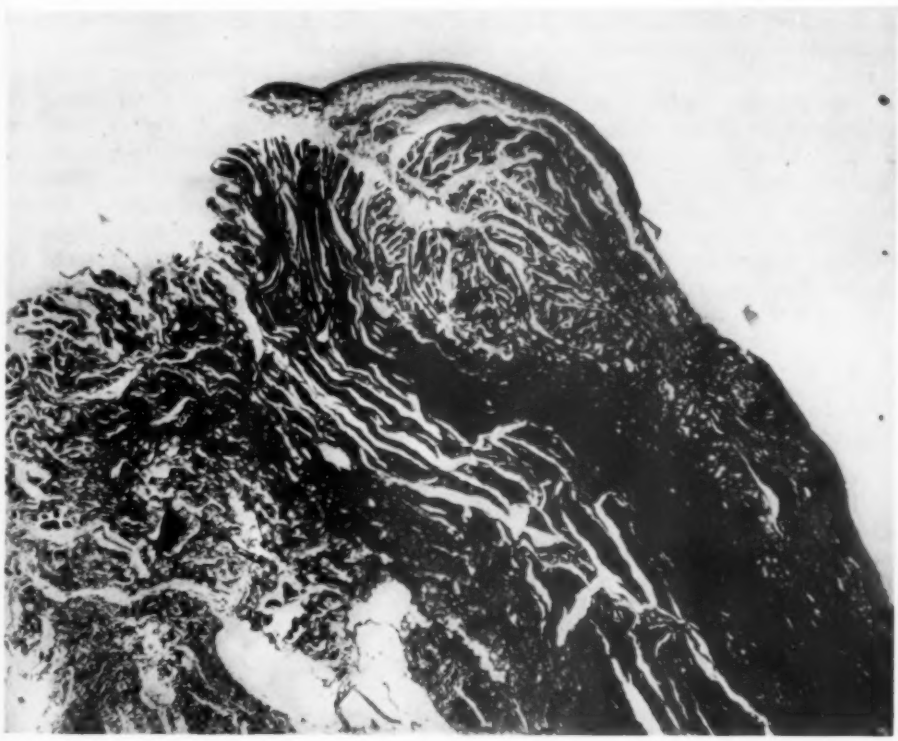

FIG. 3.

FIGS. 1, 2, 3. Representative sections from the esophagus showing cellular infiltration, excessive development of mucous glands, denudation of epithelium and hypertrophy of the *muscularis externa.*

Microscopic Examination. Sections from the liver and spleen showed no change in structure. The wall of the stomach and small intestine had areas of hemorrhage beneath the epithelial lining, occasionally under the serosa and in the smooth muscle, but presented no other recognized change.

Mucous glands were plentiful in the sections from three blocks of tissue taken from the wall of the inflamed upper end of the esophagus. Cardiac type glands were scarce. There was no keratinization of the stratified squamous epithelium. The mucous and submucous layers were not atrophied but broken and denuded areas were clearly evident. Numerous oval islands (1 by 2 by 3 mm.), predominantly of lymphocytes but with scattered plasma cells and polymorphonuclear leukocytes, lay beneath the epithelium. The muscular wall was of increased width, varying

from 3 to 6 mm., and showed excess fatty areolar tissue between the irregularly interlacing longitudinal and circular fascicles of striated muscle. Staining by Bielschowsky's silver method revealed no obvious change in the ganglia or fine network of nerves.

Dr. G. W. Rake,[21] who, with Hurst, originally described lesions in Auerbach's plexus at the middle and lower levels of the esophagus from patients having long standing achalasia of the cardia, has been kind enough to examine representative sections from the case under consideration. He stated in a personal communication, "I . . . can find no lesions of the plexus or nerves. This, of course, does not rule out such lesions entirely since in milder degrees of achalasia one may find many normal Auerbach's plexuses to one abnormal one. My experience with cases of the Plummer-Vinson syndrome has been limited, but the one case which I have examined with care microscopically showed no lesions of the nervous mechanism."

The authors are likewise indebted to Dr. Walter Brandes of the Pathological Institute of the University of Tennessee who, after examining the sections, reported, "A definite inflammatory reaction is present with moderate fibrosis and infiltration with lymphocytes. Also an infiltration with fat seems to be present in some areas in the musculature. It seems to me there are a rather large number of mucous glands present. They are unaltered except that in some areas there is a chronic inflammatory reaction as mentioned. The nerves that are seen in the sections I do not feel are noticeably altered. I do believe there is definite chronic esophagitis with erosion of the epithelial lining."

SUMMARY

The particularities of the syndrome of dysphagia and anemia, as observed by many authors, are noted. There is no proved pathological basis for the disorder. As such patients rarely come to the postmortem table, detailed gross and histological findings in one available case seem to be of more than passing interest.

Acknowledgment is made to Dr. Angus K. Wilson, Davis Memorial Hospital, for preparation of the sections and to Mr. Boyers M. Clark, Elkins, West Va., for the photomicrographs.

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EDITORIAL

PULMONARY EMBOLISM

If anything is to be accomplished in the prevention and treatment of pulmonary embolism, several things are necessary. A much keener appreciation of its frequency, a knowledge of the chief circumstances that favor its occurrence, an ability to recognize it in its mild and nonfatal forms, and an aggressive and systematic program aimed at prevention, are essential minimal requirements.

The incidence of fatal pulmonary embolism in unselected consecutive postmortem examinations is above 2 per cent.[7, 13] Pulmonary embolism accounts for from 5 to 6 per cent of deaths following surgical procedures.[12, 13] In McCartney's series it accounted for about 5 per cent of deaths in parturition, for 3.32 per cent of deaths following trauma, and for slightly less than 2 per cent of all medical deaths.[13]

While the cause or causes of pulmonary embolism are still unknown, valuable studies have been made which indicate important factors in its production. Some of these seem capable of being attacked. These studies serve to identify the circumstances under which pulmonary embolism is likely to occur, and they thus permit us to concentrate our efforts on these groups. Pulmonary embolism is encountered chiefly in patients over 40 years of age.[2] Abdominal surgery in general, and certain types of abdominal operations in particular, predispose to pulmonary embolism.[2] Fatal pulmonary embolism is approximately twice as common among patients with cardiac disease as among patients with normal hearts.[5, 13] Obesity has been shown to be an important factor predisposing to fatal pulmonary embolism.[16]

Pulmonary embolism rarely is due to detachment of the thrombus of thrombophlebitis.[2] Conversely, when pulmonary embolism occurs, seldom are there signs of peripheral phlebitis. The commonest sites of thrombi giving rise to emboli are, in order of frequency, the iliac vein, the femoral vein, the pelvic veins, the prostatic plexus, the vena cava, and the right auricle.[12] The infrequency with which an embolus arises in an upper extremity is striking in contrast to the lower extremity. The effect of gravity, and the much greater motility of the upper extremity, maintaining good venous pressure and promoting good venous blood flow, must be of paramount importance in accounting for this difference. Infection in the pelvic veins, thrombi produced by operations on the pelvic structures, which may extend into larger adjacent veins, and the fact that the venous return flow in the lower extremities is the first to suffer in any impairment of the circulation,[6] are other factors accounting for the incidence of thrombosis in the lower extremities.

No exact knowledge is available to indicate the time at which a thrombus forms after operation. One suspects that the first 48 hours is a fruitful

period for thrombus formation. The systemic blood pressure is usually lowest during that period. Maximal immobilization of the trunk and legs occurs then. Fever, in itself capable of increasing the circulatory rate, usually is slight or has not appeared during that period. Can an embolus formed at that time be in situ for eight to ten days, the usual date at which fatal pulmonary embolism occurs? It is possible that during that period the embolus is slowly increasing in size, and because of its size and the increased force of the venous flow attendant upon increased activity at the eighth or tenth day, it is carried to the lung. On the other hand it may be that changes in the blood favoring coagulation [8] reach their maximum from the sixth to the tenth day and determine the time of thrombosis and embolism. Actually, a combination of the factors of slowed venous return and alterations in the coagulating properties of the blood may constitute the most reasonable explanation.[8]

It is customary to regard marked dyspnea and cyanosis as the classical signs of pulmonary embolism. Dogmatic adherence to this conception results in failure to recognize many instances of this complication. Pulmonary embolism manifests itself frequently by the picture of shock. This is characterized by faintness, pallor, sweating, acceleration of the pulse, a marked fall in blood pressure, and sometimes by vomiting and collapse. A brief experience with pulmonary embolism teaches one that fatal attacks are preceded very frequently by milder, nonfatal seizures. The recognition of these premonitory attacks furnishes an incentive to vigorous attempts to prevent further attacks, and to increased caution in the patient's subsequent management. Certain electrocardiographic changes have been described which may assist greatly in the diagnosis of pulmonary embolism, and especially in its differentiation from acute coronary thrombosis.[3, 4, 14] The patient who gives a history of previous pulmonary embolism following an operation calls for unusual care following subsequent surgical procedures. Even more than special categories of patients shown previously to have a high degree of liability to embolism, this group of patients with premonitory seizures warrants the most intensive studies in prevention.

On the basis that impaired venous circulation plays an important rôle in the occurrence of pulmonary embolism, the following postoperative regimen has been instituted by Gray and MacKenzie.[11] The patient is placed in the Trendelenburg position for the first 24 hours after operation. Frequent inhalation of carbon dioxide, day and night during the first 48 hours, is instituted. Deep breathing exercises and encouragement of coughing are stressed. Extreme care is taken to keep the patient's legs warm at all times. Frequent massage of the legs is practiced during the first 48 hours and twice daily thereafter until the patient is out of bed. Passive and active movements of the extremities are carried out frequently during the time the patient is in bed. Attention to these details is especially important during the first 48 hours after operation. Experience to date [4]

with this program encourages the belief that it is effective in preventing fatal pulmonary embolism.*

The occurrence of a mild attack would seem to be a favorable setting for a trial of heparin. Whether a previous mild attack constitutes a contraindication to the continuation of the foregoing postoperative program, time alone will tell.

Why does death occur from pulmonary embolism? Arterial obliteration and insufficiency of the pulmonary circulation in the area involved are not satisfactory explanations. Reflex sympathetic inhibition was regarded by Villaret, Justin-Besancon and Bardin [17] as being an important mechanism. Gosset, Bertrand and Patel [10] submitted evidence that an embolus lodged in a peripheral vessel is fixed by arterial spasm. The rôle such a mechanism plays in the arterial insufficiency in arterial embolism has been discussed at length by McKechnie and Allen.[15] Is it not possible that pulmonary embolism results in spasm of some or all of the pulmonary arteries, thus explaining in part its serious consequences? On this ground, and on the basis of favorable results seen from its administration in embolic occlusion of the peripheral arteries,[1, 9] papaverine hydrochloride, grains ½, might justifiably be administered intravenously immediately after a seizure suspected of being pulmonary embolism.

There are many unknowns in this complex problem, and this seems to have given rise to a feeling of impotency in attacking the situation that has stifled progress. There is reason to hope that if we utilize such knowledge as we now possess, as well as the results of future investigations, means will be found to diminish greatly this menace.

A. R. B.

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* It is particularly difficult to evaluate the results of a program of prevention and treatment since fatal pulmonary embolism occurs in only 0.15 per cent of all operations and in 0.35 per cent of operations on the abdomen.[2]

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REVIEWS

Heart Failure. By ARTHUR M. FISHBERG, M.D., Associate in Medicine, Mount Sinai Hospital, New York City. 788 pages; 15.5 × 24 cm. Lea and Febiger, Philadelphia. 1937. Price, $8.50.

It is of course impossible to review in detail the subject matter of a book of this size. In 37 chapters the author discusses the phenomena of heart failure, peripheral circulatory failure and what he chooses to call hypodiastolic failure. In this last group are included those instances of inadequate diastolic filling of the heart such as may occur in pericarditis or tachycardia. In general he follows a scheme in which a symptom is described, the circumstances under which it occurs are explained, and the mechanisms involved in its production are discussed; descriptions of pathological anatomy are included when indicated. Left- and right-sided heart failure and failure initiated by "generalized cardiac strain" are discussed separately. The treatment of heart failure in general and in its special manifestations is discussed in further chapters. The literature pertaining to various aspects of the problems discussed has been reviewed and a bibliography is placed at the end of each chapter.

If it is kept in mind that further knowledge may modify the opinions expressed, this volume should serve excellently as a rather detailed examination of the subject.

W. S. L., JR.

External Diseases of the Eye. By D. T. ATKINSON, M.D., F.A.C.S. Second Edition. 718 pages; 15.5 × 24 cm. Lea and Febiger, Philadelphia. 1937. Price, $8.00.

This book, revised by the author, is the second edition, the first having been published by Lea and Febiger in 1934. Like the original, this edition is not limited to external diseases of the eye but includes those other conditions which may be diagnosed without the aid of the ophthalmoscope. The contents are divided into 15 chapters. Included in the chapter on diseases of the orbit is a consideration of nasal and sinus diseases which may secondarily involve the eye. As in the first edition many of the illustrations are of wax models, and while the majority of these are quite good, photographs of the actual lesion, especially if in stereopticon, would give a much better impression of the condition.

Valuable additions include description of slit-lamp microscopy, orthoptic training, allergic manifestations and some of the newer surgical procedures. Also included but rather underrated in value is the iridencleisis operation for glaucoma.

To the student, the general practitioner and the ophthalmologist this book certainly can be recommended.

H. F. G.

Appendicitis; a Clinical Study. By W. H. BOWEN, Hon. M.A. (Camb.), M.S. (Lond.), F.R.C.S. 201 pages; 13 × 19 cm. Cambridge University Press, London; Macmillan Co., New York. 1937. Price, $2.50.

An interesting monograph by an English surgeon on acute and chronic appendicitis. The author advises immediate operation in the acute stage and sets up definite rules to govern the decision as to operation in the chronic stage. The author rightly stresses the importance of a knowledge of the macroscopic pathology of the appendix. The monograph is well written but does not constitute an important advance.

T. R. A.

Handbook of Orthopaedic Surgery. By ALFRED RIVES SHANDS, JR., B.A., M.D. 593 pages; 15 × 24 cm. C. V. Mosby Company, St. Louis. 1937. Price, $5.00.

This book by Dr. Shands has been compiled to act as a ready reference book for advanced students and practitioners so that concise information may be at hand. No attempt has been made to go into details of description and analysis of the many problems, but rather to give the essentials of all orthopaedic conditions and to allow the investigator to proceed further in articles referred to in the bibliography. If this book is used for students in school, explanatory lectures should be used to supplement it. The bibliography is quite general and complete and offers opportunity for further intensive study of any subject.

A. F. V.

Textbook of Diagnostic Roentgenology. By LEWIS J. FRIEDMAN, M.D. 623 pages; 17 × 25 cm. D. Appleton-Century Co., New York. 1937. Price, $10.00.

This volume attempts to cover the whole field of diagnostic roentgenology and hence deals with each aspect in too brief a fashion to serve the purpose of the man specializing in that field. It is perhaps best suited to give the physician in general practice a survey of the whole subject.

The viewpoint is consistently maintained that the roentgenologist is a medical consultant and should be in possession of all available clinical data before rendering his opinion.

W. L. K.

Carcinoma of the Female Genital Organs. By M. C. MALINOWSKY, and E. QUATER. Translated from the Russian by A. S. Schwartzmann, A.B., M.D. 255 pages; 15.5 × 23.5 cm. Bruce Humphries, Inc., Boston. 1936. Price, $5.00.

This work is a rather superficial one covering all phases of carcinoma of the female sexual organs. It is contributed to by eleven different authors, and contains much interesting statistical data compiled chiefly from the European clinics and from the works of outstanding European investigators. It is interesting to note throughout this work the similarity of the treatment of these types of carcinoma in Europe and in this country It is surprising, however, that no mention is made of the use of spinal alcohol injections in the treatment of pelvic pain in far advanced cases.

The chapter on the "Clinical Picture of Carcinoma of the Uterus" by Dr. Quater, and the one on "Metastatic Carcinoma of the Ovaries" by Dr. Pojarissky are particularly good. The last chapter in the book deals with carcinoma of the female sexual organs from the viewpoint of disability and social insurance. The illustrations throughout the book, especially the microphotographs, are quite poor.

This work would be much more valuable if it were more exhaustive.

J. C. D.

COLLEGE NEWS NOTES

Nominations, 1938–39

Elective Offices

Dr. William J. Kerr, President-Elect, San Francisco, Calif., accedes to the Presidency.

New Nominations

President-Elect ..... O. H. Perry Pepper, Philadelphia, Pa.
First Vice-President ..... James B. Herrick, Chicago, Ill.
Second Vice-President ..... Noble Wiley Jones, Portland, Oregon
Third Vice-President ..... Charles T. Stone, Galveston, Tex.

Respectfully submitted,

Committee on Nominations,
Jonathan C. Meakins, *Chairman*

Notice of Amendment to the By-Laws

In accordance with the present By-Laws of the American College of Physicians and by direction of the Board of Regents at a regular meeting held on April 18, 1937, notice is hereby given to the Fellows and Masters of the College that the following amendment to the By-Laws has been approved by said Board of Regents and will be presented for adoption or rejection at the Annual Business Meeting to be held in New York City April 7, 1938:

(An addition to the By-Laws, Article IV, Section 1, to be added as an additional paragraph)

"Any member of the Board of Governors unable to attend the Annual Session shall appoint as his alternate, with all the privileges of a Governor, a Master or Fellow of his district who will be in attendance at that Session. Upon presentation to the Chairman of the Board of Governors of a certificate of appointment, the alternate shall be recognized and act in the full capacity of Governor for the Session to which he has been appointed. The same alternate shall not be appointed for more than two consecutive years."

New Life Members

The following Fellows have been entered, upon their subscriptions, as Life Members of the American College of Physicians, at the dates indicated, making a total of ninety-four.

Dr. Louis H. Fligman, Helena, Mont., January 10, 1938
Dr. Max. H. Weinberg, Pittsburgh, Pa., January 13, 1938
Dr. W. P. Anderton, New York, N. Y., January 13, 1938
Dr. Orrin Sage Wightman, New York, N. Y., January 15, 1938
Dr. J. Dorwin Mabey, Montclair, N. J., January 15, 1938
Dr. Robert L. Levy, New York, N. Y., January 15, 1938
Dr. Harry S. Emery, Portland, Maine, January 17, 1938
Dr. Alex. M. Burgess, Providence, R. I., January 18, 1938

Dr. Theodore S. Bacon, Springfield, Mass., January 19, 1938
Dr. Mary Riggs Noble, Bowmansdale, Pa., January 24, 1938
Dr. Mary Elizabeth Bass, New Orleans, La., January 24, 1938
Dr. Karl Vogel, New York, N. Y., January 25, 1938

Gifts to the College Library

Grateful acknowledgment is made of the receipt of the following donations to the College Library of publications by members:

Books

Dr. Linn J. Boyd (Fellow), New York, N. Y.—"A Study of the Simile in Medicine";
Dr. Thomas Hall Shastid (Fellow), Duluth, Minn.—"Tramping to Failure" and "How to Stop War-Time Profiteering";
Dr. William D. Stroud (Fellow), Philadelphia, Pa., co-author with Dr. Lawrason Brown (Fellow, deceased), Dr. George R. Minot (Fellow), Dr. William B. Castle (Fellow), Dr. George B. Eusterman (Fellow) and Dr. George F. Dick—an autographed copy of each of the 1934, 1935 and 1936 "Year Book of General Medicine";
Dr. Russell M. Wilder (Fellow), Rochester, Minn.—an autographed copy of "A Primer for Diabetic Patients";
Dr. Lowell S. Selling (Associate), Detroit, Mich.—"Diagnostic Criminology."

Reprints

Major Joseph R. Darnall (Fellow), (MC), U. S. A.—2 reprints;
Dr. Ralph M. Fellows (Fellow), Osawatomie, Kan.—2 reprints;
Lt. Col. Arthur R. Gaines (Fellow), (MC), U. S. A.—1 reprint;
Dr. Paul John Hanzlik (Fellow), San Francisco, Calif.—51 reprints;
Dr. Edward G. Huber (Fellow), Boston, Mass.—1 reprint;
Dr. George Morris Lewis (Fellow), New York, N. Y.—25 reprints;
Dr. James L. McCartney (Fellow), Catskill, N. Y.—1 reprint;
Dr. Joseph A. Pollia (Fellow), Los Angeles, Calif.—14 reprints;
Dr. Thomas Hall Shastid (Fellow), Duluth, Minn.—2 reprints;
Dr. Virgil E. Simpson (Fellow), Louisville, Ky.—1 reprint;
Dr. Walter M. Simpson (Fellow), Dayton, Ohio—3 reprints;
Dr. William L. Smith (Fellow), New Orleans, La.—1 reprint;
Dr. Felix Cunha (Associate), San Francisco, Calif.—10 reprints;
Dr. Herbert R. Edwards (Associate), New York, N. Y.—4 reprints;
Dr. Hyman I. Goldstein (Associate), Camden, N. J.—1 reprint;
Dr. John M. Nicklas (Associate), Valhalla, N. Y.—2 reprints;
Dr. Lowell S. Selling (Associate), Detroit, Mich.—18 reprints.

Dr. C. W. Waddell (Fellow), Fairmont, W. Va., has contributed two original copies of the "Annals of Medicine," Volume I, Nos. 1 and 2, to the permanent archives of the College. These were the first two journals sponsored and published by the College.

Grateful acknowledgment is also made of the receipt of the following gifts:

Mr. and Mrs. James Inglis, Ann Arbor, Mich.—1 book, "The Collapse Therapy of Pulmonary Tuberculosis" by John Alexander, M.D.

Metropolitan Life Insurance Company, New York, N. Y.—1 book, "Twenty-Five Years of Health Progress, A Study of the Mortality Experience Among the Industrial Policyholders of the Metropolitan Life Insurance Company, 1911 to 1935."

Sectional Meeting of Arkansas Members

Dr. Oliver C. Melson (Fellow and Governor for Arkansas) reports that the Fellows and Associates of the American College of Physicians of Arkansas met at the Albert Pike Hotel in Little Rock on November 8. Dr. John H. Musser (Fellow), New Orleans, was the guest speaker. Those present included Dr. H. T. Smith of McGehee; Dr. F. N. Gordon of Fayetteville; Dr. George B. Fletcher, Dr. A. G. Sullivan and Dr. Euclid Smith of Hot Springs; Dr. Charles T. Chamberlain of Fort Smith; Dr. L. D. Massey of Osceola; Dr. J. D. Riley of State Sanatorium; Dr. A. A. Blair of Fort Smith; Dr. J. N. Compton, Dr. John R. Dibrell and Dr. Oliver C. Melson of Little Rock.

Such state meetings will be inaugurated as a yearly feature in Arkansas.

Dr. John G. Young (Fellow), Dallas, Tex., is President of the Texas Pediatric Society and of the Dallas Pediatric Society. Dr. Young is also Consultant to the Dallas Tuberculosis Association and Chief of the Medical Staff of Freeman Memorial Clinic for Children.

Dr. Howard S. Brasted (Fellow), Hornell, N. Y., addressed the Pre-Medic Club of Haughton College recently on "Blood Transfusions and Blood Typing."

Dr. J. W. Torbett, Sr. (Fellow), Marlin, Texas, gave a lecture on "Undulant Fever of the Chronic Types" before the Brown-Mills and San Saba County Medical Society meeting in November. Dr. Torbett is director and one of the founders of the Marlin Hot Wells Foundation, which recently established the Crippled Children's Hospital and Hot Water Pool in Marlin, Texas.

Dr. E. W. Gehring (Fellow and Governor for Maine), having recently resigned as Chief of Medical Service of Maine General Hospital at Portland, has been succeeded by Dr. E. H. Drake (Fellow).

Dr. B. S. Pollak (Fellow) is the medical director of the new Hudson County Tuberculosis Hospital and Sanatorium, newest unit of the Jersey City Medical Center. This hospital, towering some eighteen or twenty stories, will accommodate 510 patients. In equipment, furniture and facilities, nothing has been spared to make the institution one of the most complete in the country.

At the Annual Congress of the Council on Medical Education and Hospitals of the American Medical Association, to be held in Chicago, February 14 and 15, 1938, the following Fellows of the College will participate:

Dr. Willard C. Rappleye, Dean of Columbia University College of Physicians and Surgeons, New York City, "The Functions of the Special Examining Boards";

Dr. Burrell O. Raulston, Professor of Medicine, University of Southern California School of Medicine, Los Angeles, "An Introduction to Clinical Medicine and Some Variations in the Curriculum of the Third and Fourth Years in Medical School";

Dr. J. G. FitzGerald, Director of the School of Hygiene and Connaught Laboratories, University of Toronto, Toronto, Ont., Canada, "Medical Student Instruction in Preventive Medicine";

Dr. John H. Musser, Professor of Medicine, Tulane University of Louisiana School of Medicine, New Orleans, and Dr. James D. Bruce, Director of the Department of Postgraduate Medicine, University of Michigan, Ann Arbor, participants in the Symposium on Graduate Medical Education.

Dr. Herbert L. Bryans (Fellow), Pensacola, Fla., has been elected President of the Gulf Coast Clinical Society.

The Bronx Hospital of New York City sponsored a series of afternoon lectures for physicians during November and December. Dr. Alvan L. Barach (Fellow), New York City, presented an address on "Peripheral Circulatory Failure and Acute Pulmonary Edema Occurring as Complications in Pneumonia"; Dr. Elliott P. Joslin (Fellow), Boston, "Diabetes Mellitus"; and Dr. Russell L. Cecil (Fellow), New York City, "Chronic Arthritis."

Dr. Samuel M. Bittinger (Fellow) has been appointed assistant superintendent and medical director of the new sanatorium for the treatment of tuberculosis at Black Mountain, N. C.

The Commonwealth Fund of New York has approved a grant of $10,857 annually for three years to Western Reserve University School of Medicine, Cleveland, especially for research on chronic nephritis by Dr. Joseph M. Hayman (Fellow), who is associate professor of medicine.

At the last annual meeting of the Medical Society of the State of Pennsylvania, the Board of Trustees and the past presidents presented to Dr. Walter F. Donaldson (Fellow), Pittsburgh, Secretary of the Society for many years, an oil portrait of himself. Dr. Arthur C. Morgan (Fellow), Philadelphia, made the presentation address.

Dr. William Egbert Robertson (Fellow), Philadelphia, presented an address, "Dr. Rush and the Signers of the Constitution," before the Philadelphia County Medical Society on the occasion of the marking of the one hundred and fiftieth anniversary of the signing of the Constitution of the United States.

Dr. Charles S. Holbrook (Fellow), New Orleans, has been elected President-Elect of the Southern Psychiatric Association.

Dr. Priscilla White (Fellow), Boston, addressed the fifth annual scientific meeting of the Georgia Pediatric Society at Atlanta on December 9 on "Endocrine Problems in Juvenile Diabetes; Recent Problems in Juvenile Diabetes."

Dr. George G. Ornstein (Fellow), New York City, delivered a paper on "The Pathogenesis of Pulmonary Tuberculosis from the Physician's Point of View" in connection with the fall graduate conferences of the Wayne County (Michigan) Medical Society, the Detroit Department of Health and the Detroit Tuberculosis Sanatorium.

Dr. Irving S. Wright (Fellow), New York City, was a guest speaker at the annual "Scientific Day" of Montefiore Hospital, Pittsburgh, recently, his address being on "A Critical Analysis of Recent Advances in the Study of Vascular Disease."

Dr. David P. Barr (Fellow), St. Louis, Dr. Russell L. Cecil (Fellow), New York City, Dr. Alfred Friedlander (Fellow), Cincinnati, Dr. Ernest E. Irons (Fellow), Chicago, and Dr. Roger I. Lee (Fellow), Boston, are members of the Advisory Committee on Pneumonia Control, recently appointed by Dr. Thomas Parran (Fellow), Surgeon General of the U. S. Public Health Service.

Dr. Charles C. Bass (Fellow), Dean of Tulane University of Louisiana School of Medicine, delivered the principal address at the recent dedication of the Rudolph Matas Medical Library, which is the library of Tulane University of Louisiana School of Medicine, named in honor of Dr. Rudolph Matas, Emeritus Professor of Surgery at the University.

Dr. Henry A. Christian (Fellow), Boston, Mass., was one of the speakers at the dedication of the new building of the Syracuse University College of Medicine, Syracuse, N. Y., on November 22.

Dr. Clarence E. de la Chapelle (Fellow), New York City, is acting chairman of the Department of Medicine of the New York University College of Medicine.

Dr. James Edward Hubbard (Associate), is the director of the Huntington (W. Va.) Radium and X-Ray Clinic, which recently opened new quarters in the Memorial Hospital at Huntington.

Dr. Lee Rice (Fellow), San Antonio, Texas, has been elected a vice-president of the Southern Medical Association.

Among speakers from the United States on the seventh cruise congress of the Pan American Medical Association, which left New York City January 15 were the following:

Dr. Edwin C. Ernst (Fellow), St. Louis, "Recent Developments in Relation to the Radiation Management of Cancer";
Dr. Howard R. Hartman (Fellow), Rochester, Minn., "Treatment of Hemorrhagic Ulcer of Stomach or Duodenum";
Dr. Herman N. Bundesen (Fellow), Chicago, Ill., "Amebiasis."

The Section on the Medical Sciences of the American Association for the Advancement of Science devoted its entire program, December 27 to January 1, to a symposium on syphilis. The following were contributors:

Dr. John A. Kolmer (Fellow), Philadelphia, "Serologic Reactions in Relation to Infection and Treatment of Syphilis";
Dr. Paul A. O'Leary (Fellow), Rochester, Minn., "Neurosyphilis";
Dr. Walter M. Simpson (Fellow), Dayton, Ohio, "High Temperatures";
Dr. Dudley C. Smith (Fellow), University, Va., "Untoward Reactions—Intercurrent Infections";
Dr. Thomas Parran (Fellow), Washington, D. C., "Syphilis: A Public Health Program."

Dr. Solomon Strouse (Fellow), formerly of Chicago, has been appointed Associate Clinical Professor of Medicine at the University of Southern California Medical School at Los Angeles.

As a recognition of his medical and public health services to Cuba, the Order of Merit of Carlos Finlay was recently conferred upon Dr. Edgar Mayer (Fellow), New York City.

Dr. C. C. Carpenter (Fellow), Dean of the Wake Forest Medical School, will be the director of the new school of medical technology, recently announced by Wake Forest College and the Rex Hospital, of Raleigh, N. C.

Dr. O. H. Perry Pepper (Fellow), Philadelphia, was a guest speaker and guest clinician on the program of the William Moore Guilford Clinic, a newly organized graduate clinic day, observed by the Good Samaritan Hospital, Lebanon, Pa., and the Lebanon County Medical Society, each year during the week of Dr. Guilford's birthday. Dr. Guilford reached the age of 105 years on November 26, 1937.

Dr. C. Lydon Harrell (Fellow), Norfolk, will serve as medical adviser of the new Tidewater Victory Memorial Hospital for the treatment of tuberculosis near Norfolk.

Dr. Herbert Z. Giffin (Fellow), Professor of Medicine in the University of Minnesota Graduate School of Medicine, has been elected President of the Staff of the Mayo Clinic.

Dr. G. Harlan Wells (Fellow), Philadelphia, has been elected President of the Homeopathic Medical Society of Pennsylvania.

OBITUARIES

DR. LAWRASON BROWN

Dr. Lawrason Brown (Fellow) died at his home in Saranac Lake, December 26, 1937, at the age of sixty-six. He had been ill at periods for the past several years with symptoms traceable to longstanding pulmonary tuberculosis. Mrs. Brown survives him.

Dr. Brown was born in Baltimore, September 29, 1871, and there received his education. Johns Hopkins gave him the A.B. degree in 1895, and the M.D. in 1900. He soon went to Saranac Lake where he came under the influence of Trudeau. Assuming the duties of resident physician at the Trudeau Sanatorium in 1901, his great energy, efficiency and intelligence were released to build on the foundation which Trudeau had labored to lay. With zeal that grew from the spirit of truth within him and throve in the atmosphere of humaneness about him, Brown perfected the plan of treatment of tuberculous patients in the sanatorium, organized the records, instituted a follow-up system which in later years yielded rich clinical studies, and furthered scientific study in the laboratory and clinic. He soon became a leader among that remarkable group of physicians who made Saranac Lake a fountain head of knowledge of tuberculosis and established a standard of clinical practice which was the pattern for the country. The national antituberculosis campaign was gaining momentum and, as a part of this, the need for sanatoria became more and more apparent, largely on account of what was being demonstrated at the Trudeau Sanatorium. As these were established throughout the country, Brown's influence spread afar. He conceived the idea of organizing physicians engaged in sanatorium work, and this fructified in the creation of the American Sanatorium Association, now grown to be the most important society of its kind in the country. He established and edited the *Journal of the Outdoor Life,* bringing to tuberculous patients the essential facts of hygiene and proclaiming the creed of acquiescence and hope which is a vital part of the "cure." For thousands of these patients his "Rules for Recovery from Tuberculosis" was and still is a lamp in the darkness. An unfailing scientific curiosity constantly renewed his energy which he spent freely in discussions with his confreres at informal and formal meetings, in teaching, and in writing numerous articles for periodicals, books and systems of medicine, as well as longer monographs. It was his habit always to keep testing and retesting medical principles, mostly in the light of the Trudeau follow-up system and its revelation of the ultimate fate of his former patients, the result of which was a progressive refinement of the understanding of the behavior of tuberculosis and its diagnosis and treatment. The soundness of his understanding, the honesty of his thinking, and the quality of his leadership won for Brown a degree of respect and distinction enjoyed by few in their chosen medical fields. His long experience and deep knowledge enabled

him to evaluate better than most physicians the factors which aid the healing of tuberculosis, and among these he always assigned a high place to the *vis medicatrix naturae*. He deprecated ignorance of the possibilities of rest treatment and the fallacy of attempting to displace it completely with "collapse" therapy, though he did not underrate the latter. Rather, he exemplified that discriminating judgment in selecting a plan of treatment for the individual patient which marks the seasoned clinician.

At the time of his death, Dr. Brown was consultant to the Trudeau Sanatorium and the Waverly Hills Sanatorium, Louisville, Ky.; also a trustee of the Trudeau Sanatorium, the New York State Hospital at Ray Brook, and the Potts Memorial Hospital, Livingston, N. Y., and a member of the advisory council of the Henry Phipps Institute, Philadelphia. He had been president of the American Sanatorium Association, American Clinical and Climatological Association, and the National Tuberculosis Association. He was a fellow and life member of the American College of Physicians, and a member of the Association of American Physicians, the American Association of Thoracic Surgery, and of other organizations. He received the Trudeau medal from the National Tuberculosis Association in 1933. He was awarded the honorary degree of doctor of science from Dartmouth College in 1931 and from the Medical College of Virginia in 1936.

Lawrason Brown had the devotion of his patients, the respect of his professional brethren, and the love of his friends.

J. Burns Amberson, Jr., M.D., F.A.C.P.

DR. JOHN LEE

Dr. John Lee of Detroit died September 22, 1937, after a long illness.

Dr. Lee was born in Detroit in 1869, and graduated from the Detroit College of Medicine in 1890. For many years he taught as Assistant Professor of Medicine at his alma mater, his active clinical teaching being done at St. Mary's Hospital, where he served throughout his long professional career as Attending Physician in the Department of Medicine. Dr. Lee served during the Spanish American War. He had been an Associate of the American College of Physicians for many years.

From the time that he started in practice, Dr. Lee devoted a large part of his time to teaching in the wards at St. Mary's Hospital, as well as carrying on a large practice. Energetic and enthusiastic, he enjoyed the warm friendship and respect of the many physicians who owed their clinical training to him during their college careers.

Henry R. Carstens, M.D., F.A.C.P.,
Governor for Michigan.

DR. ALBERT WARREN FERRIS

Dr. Albert Warren Ferris (Fellow), East Orange, N. J., died October 4, 1937, following a prolonged illness of encephalitis with a parkinsonian syndrome, at the age of 81.

Dr. Ferris was born in Brooklyn, N. Y., 1856; attended Adelphi Academy of Brooklyn, Newark Academy, Newark Latin School and Hasbronck Institute of Jersey City; A.B., New York University, 1878; A.M., same, 1885; M.D., Columbia University College of Physicians and Surgeons, 1882; interned at Kings County Hospital, Flatbush, L. I., 1883–85; assistant and later resident physician, Sanford Hall for Insane, Flushing, N. Y., 1885–91; physician-in-charge, Dr. Choate's Home for Insane, Pleasantville, N. Y., 1906–07; senior resident physician, Glen Springs Sanitarium, Watkins, N. Y., 1912–13 and from 1917 to 1930; president, New York State Commission on Lunacy, 1907–11 (appointed by former Governor Charles E. Hughes); medical expert and director, Saratoga Springs State Reservation Commission, 1913–16; for some time consulting physician to the Binghamton State and Manhattan State (N. Y.) hospitals; also during his earlier career, Assistant in Neurology, Vanderbilt Clinic, Columbia University, 1893–1900; member, Phi Beta Kappa and Delta Upsilon fraternities (national first vice president of latter in 1884 and in 1902); member and ex-vice president, ex-editor of journal and a delegate to the American Medical Association from the Medical Society of the State of New York; Fellow and ex-chairman of a section, New York Academy of Medicine; member, American Psychiatric Association; Fellow, American Medical Association; member of various New York county medical societies, according to his residence at the time; author of many articles in national medical journals and of over 250 articles appearing in the International Encyclopedia and in the International Year Book; Fellow of the American College of Physicians since 1920.

Dr. Ferris is survived by a brother, Mr. Richard Ferris, New York City.

Seldom does one see more evidence of a fruitful professional life. His career was an honor to the medical profession and to the College.

CLARENCE L. ANDREWS, M.D., F.A.C.P.,
Governor for New Jersey.

DR. E. MARK HOUGHTON

Dr. E. Mark Houghton of Detroit, Michigan, died December 12, 1937.

Born in 1867, he was educated at the University of Michigan, where he received his Ph.C. degree in 1893, and M.D. in 1894. After further work in pharmacology, he joined the staff of Parke, Davis and Company in 1895, where he became director of medical research and biological laboratories. He held this position until 1929, when he was made consulting director.

Besides membership in the Wayne County Medical Society, Detroit

Medical Club, Michigan State Medical Society, and American Medical Association, he held membership in the Society of American Bacteriologists, American Pharmaceutical Association, Society of Immunologists, National Tuberculosis Association, and in 1910 was a delegate to the United States Pharmacopoeia Convention. Dr. Houghton had been a Fellow of the American College of Physicians since 1921.

Enjoying a high reputation for work in his professional field, Dr. Houghton was also a genial friend to his many professional colleagues. A scholarly gentleman, he will be greatly missed by his many friends both in the profession and the laity.

HENRY R. CARSTENS, M.D., F.A.C.P.,
Governor for Michigan.

DR. HARVEY ELIJAH WELLMAN

On October 20, 1937, Dr. Harvey E. Wellman died at the Jane Brown Memorial Hospital at Providence as the result of an acute duodenitis and enteritis of eight days' duration.

Dr. Wellman, a Fellow of the College (1937), had earned the deep respect and affection of his colleagues and of the patients who had come under his care. Always an earnest and capable clinician, a most conscientious worker in his various hospital assignments, he found time for an interest in the broader aspects of medical study and always had a keen eye for the improvement of the service in the various hospital organizations with which he was connected. During his term as Resident Physician at the Rhode Island Hospital he was particularly interested in the Pathological Laboratory and as a result of his efforts a radical improvement in this department took place. As Assistant Physician in the Division of University Health at Brown University he won the confidence and affection of the student body. During the last few years of his life he became especially interested in diseases of the chest and his place in the Thoracic Clinics of the Charles V. Chapin and Rhode Island Hospitals will be hard to fill.

At the time of his death Dr. Wellman was forty-five years old. He was graduated from Williams College with the degree of A.B. in 1914 and from Harvard Medical School in 1926. He served with the U. S. Navy Base Hospital No. 4 during the World War. He was appointed Assistant Visiting Physician to the Rhode Island Hospital in 1936, Visiting Physician to the Charles V. Chapin Hospital in 1935 and Consulting Physician to the Rhode Island State Infirmary in 1935. He was a diplomate of the National Board of Medical Examiners, the author of a number of published papers and a member of the following organizations: Providence Medical Association, Rhode Island Medical Society, New England Heart Association and American Medical Association.

ALEX. M. BURGESS, M.D., F.A.C.P.,
Governor for Rhode Island.

DR. HENRY WILLIAM JAEGER

Dr. Henry William Jaeger (Associate, 1928), born March 14, 1888, at Washington, D. C., died October 21, 1937, at his home in Washington of coronary occlusion.

Dr. Jaeger was educated in the Public Schools of Washington and at the George Washington University, from which he was graduated in medicine in 1911. He served internships at Casualty Hospital, Washington, and at the German Hospital, Brooklyn, N. Y. He was a member of the Medical Society of the District of Columbia, a Fellow of the American Medical Association, and an Associate of the American College of Physicians.

Dr. Jaeger was particularly interested in music and was a member of the choir of the Nobles of the Mystic Shrine. During the last years of his life he was tenor soloist at the Washington Cathedral. He had those "mysterious motions of the soul, not to be defined save in strange melodies." Because of its illusiveness, its subtle shades, and its vanishing ecstasies, he found music entrancing.

Keeping abreast of the advances in medicine, Dr. Jaeger had a lucrative practice. His patients became his friends, because he had a capacity for a deep and sustained friendship, which he manifested not only when occasion offered, but he sought opportunities to extend to others those little amenities which are precious to all of us. He was admired and loved not only for loyalty to friendship, but also for his integrity of purpose and the sweetness of his nature, and because he was of the company of those who make the barren places fruitful with kindness.

Furnished by courtesy of The Medical Society
of the District of Columbia.

DR. THOMAS TIPTON WALKER

In the death of Thomas Tipton Walker, the medical profession loses a well qualified pathologist, a keen student of medicine, and one particularly suited to research. He proudly and meticulously followed the precepts of medical ethics and demanded of himself and his colleagues a very high standard of work and achievement. Six published papers attest his scientific interest in medicine. In his hours of recreation, he made the same demands of himself as in his work—to excel in whatever he did.

Dr. Walker was born in Atlanta, Georgia, March 11, 1904. He graduated from Emory University in 1924 with the degree of Bachelor of Science, cum laude, and the following year received his Master's degree from the University of North Carolina. He then entered Harvard Medical College and in 1928 a scholarship took him to London, where he worked at St. Thomas' Hospital under Sir Cuthburt Wallace.

On graduation from Harvard Medical College, he accepted a residency

in pathology at the Boston City Hospital, and during his stay there he instructed in physiology and pathology at Tufts Medical School until 1931. After postgraduate study abroad at Eppendorfer Krankenhaus and in Frankfurt at the Stadische Krankenhaus, he returned to the United States and accepted a position as pathologist at the Duke Hospital, Durham, North Carolina. While at Durham he was instructor in pathology at Duke University. In 1932 he became director of the Department of Laboratories at the House of the Good Samaritan and Mercy Hospitals, Watertown, New York, later being appointed consulting pathologist at the Jefferson County Sanatorium at Watertown. These positions he fulfilled most efficiently and rendered to Watertown and surrounding communities the highest type of pathological service.

He was diplomate of the National Board of Medical Examiners and also of the American Board of Pathology; a member and officer of the Jefferson County Medical Society; a member of the New York State Medical Society; the American Medical Association; the Association of Pathologists and Bacteriologists; American Society of Clinical Pathologists; the New York State Association of Public Health Laboratories; the Pathological Society of Eastern New York; and an Associate of the American College of Physicians since April 28, 1935.

Dr. Walker died November 13, 1937, and in his untimely death medicine was deprived of a research student who was well qualified to be a leader in the advance of medical science.

He is survived by his widow, Lillie Cutlar Walker.

This obituary was very kindly prepared by Walter S. Atkinson, M.D., of Watertown, New York.

C. F. Tenney, M.D., F.A.C.P.,
Governor for Eastern New York, New York.

PROGRAM
TWENTY-SECOND ANNUAL SESSION
AMERICAN COLLEGE OF PHYSICIANS
NEW YORK, N. Y.

April 4–8, 1938

GENERAL SESSIONS AND LECTURES

James H. Means, President

NEW YORK EXECUTIVE COMMITTEE

James Alexander Miller, General Chairman
James Ralph Scott, Vice-Chairman
Edward R. Loveland, Executive Secretary

Robert A. Cooke
Russell L. Cecil
Howard F. Shattuck
Peter Irving
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R. Garfield Snyder

COMMITTEE ON LADIES ENTERTAINMENT

Mrs. F. Warner Bishop, Chairman

Mrs. George C. Andrews
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Mrs. Kenneth R. McAlpin
Mrs. James Alexander Miller
Mrs. Howard F. Shattuck
Mrs. Edgar Stillman
Mrs. Kenneth Taylor
Mrs. Lucius Wilmerding

GENERAL INFORMATION

New York Headquarters

Waldorf-Astoria Hotel, 50th St. & Park Ave.

The Waldorf-Astoria Hotel will be headquarters for Officers, Regents, Governors and members of the College; also the General Headquarters for registration, technical exhibits, general scientific sessions, special lectures and round table luncheon-conferences.

List of New York Hotels (partial)	Blocks from Head-quarters	Rates per day	
		Single Room with bath	Double Room with bath
WALDORF–ASTORIA, 50th St. & Park Ave.	..	$5.00 and up	$8.00 and up
Barclay, 111 E. 48th St.	1	5.00 and up	8.00 and up
Belmont Plaza, 49th St. & Lexington Ave.	¼	3.00 and up	5.00 and up
Biltmore, 43d St. & Madison Ave.	6	4.00 and up	7.00 and up
Commodore, 42d St. & Lexington Ave.	7	3.50 and up	5.00 and up
Lexington, 48th St. & Lexington Ave.	¼	4.00 and up	6.00 and up
Murray Hill, 41st St. & Park Ave.	9	4.00 and up	3.50 inside room 5.00 outside room
Pennsylvania, 34th St. & 7th Ave.	20	3.50 and up	5.00 and up
Prince George, 14 E. 28th St.	22	2.25 to 4.00	3.50 to 6.00
Roosevelt, 45th St. & Madison Ave.	5	5.00 and up	7.00 and up
Shelton, 49th St. & Lexington Ave.	¼	3.50 and up	4.50 and up

Members should make reservations directly with hotels of their choice. Mention the convention of the American College of Physicians, for rates above quoted are, in many instances, only for this occasion.

WHO MAY REGISTER—

(*a*) All members of the American College of Physicians in good standing for 1938 (dues, if not paid previously, may be paid at the Registration Bureau).

(*b*) All newly elected members.

(*c*) House Officers of the hospitals participating in the program, without registration fee, upon presentation of proper identification; exhibits, general sessions and afternoon lectures.

(*d*) Members of the Medical Corps of Public Services of the United States and Canada, without registration fee, upon presentation of proper credentials.

(*e*) Qualified physicians who may wish to attend this Session as visitors. Such physicians shall pay a registration fee of $12.00, and shall be entitled to one year's subscription to the ANNALS OF INTERNAL MEDICINE (in which the proceedings will be published), included within such fee.

REGISTRATION BLANKS FOR ALL CLINICS AND DEMONSTRATIONS AND ROUND TABLE CONFERENCES will be sent with the formal program to members of the College. Guests will secure registration blanks at the Registration Bureau during the Session.

TRANSPORTATION—On account of nationwide reductions in railroad fares, there are no convention rates any longer in effect. In many instances, however, reduced round trip tickets are in effect from certain localities. Members should consult their local ticket agents.

The Committee on Transportation will issue full data concerning local transportation at the meeting.

THE GENERAL BUSINESS MEETING OF THE COLLEGE will be held at 11:30 a.m., Thursday, April 7, immediately following the general scientific program of the morning. All Masters and Fellows of the College are urged to be present.

There will be the election of Officers, Regents and Governors, the reports of the Treasurer and of the Executive Secretary, the presentation of an amendment to the By-Laws, and the induction to office of the new President, Dr. William J. Kerr, San Francisco, Calif.

BOARD AND COMMITTEE MEETINGS—The following meetings are scheduled as indicated. Special meetings will be announced and posted.

A *special dinner* will be tendered *to the Board of Regents* by members of the Board of Governors at the Waldorf-Astoria Hotel, Sunday evening, April 3.

COMMITTEE ON CREDENTIALS

Sunday, April 3, 9:00 a.m.....Carpenter Suite, Fourth Floor, Waldorf-Astoria Hotel

BOARD OF REGENTS

Carpenter Suite, Fourth Floor, Waldorf-Astoria Hotel

Sunday, April 3, 2:30 p.m.
Tuesday, April 5, 12:00 m.*
Friday, April 8, 12:00 m.*

BOARD OF GOVERNORS

Carpenter Suite, Fourth Floor, Waldorf-Astoria Hotel

Monday, April 4, 5:00 p.m.
Wednesday, April 6, 12:00 m.*

* Buffet luncheon served.

SPECIAL FEATURES

Monday, April 4, 1938

THE ANNUAL SMOKER will be held in the Ballroom of the Waldorf-Astoria Hotel on Monday, immediately following the evening meeting, at about ten-twenty o'clock. It will be limited to men only. The entertainment will consist of a floor show to be followed by informal singing by the audience. Light refreshments and beer will be served. Fellows and Associates are invited to attend the Smoker as guests of the College.

Tuesday, April 5, 1938

THEATER NIGHT. Blocks of desirable seats for some of the most popular plays have been reserved. These will be on sale at the Waldorf Ticket Agency, and those desiring to go to the theater are urged to buy their tickets promptly after registering for the Session.

Wednesday, April 6, 1938

CONVOCATION OF THE COLLEGE—8:30 p.m., Grand Ballroom, Waldorf-Astoria Hotel. All Masters and Fellows of the College and those to be received in Fellowship should be present. Newly elected Fellows who have not yet been received in Fellowship are requested to assemble in the West Foyer of the Waldorf-Astoria Hotel (third floor, adjoining west side of the Ballroom) at 7:45 o'clock, preparatory to the formation of the procession. They will occupy especially reserved seats in the central section of the Ballroom, to which they will be conducted by the Convocation marshal promptly at 8:30. It is customary for all to appear in evening dress.

The Convocation is open to all physicians and their families generally. A cordial invitation is also issued to such of the general public as may be interested.

Following the Convocation Ceremony, the President will present the John Phillips Memorial Medal for 1937–38, and will thereafter deliver the Presidential Address. Dr. Karl T. Compton, President of the Massachusetts Institute of Technology, Cambridge, Mass., will deliver the Convocational Oration, "Possibilities in Biological Engineering."

The Presidential Reception, with dancing, will follow immediately after the program in the Grand Ballroom.

Thursday, April 7, 1938

THE ANNUAL BANQUET OF THE COLLEGE will be held in the Grand Ballroom of the Waldorf-Astoria Hotel on Thursday evening at eight o'clock. Dr. James Alexander Miller, General Chairman of the Twenty-second Annual Session of the College, will be the Toastmaster. The address of the evening, "Education in a Changing World," will be delivered by Honorable John H. Finley, LL.D., Associate Editor of the New York Times. Dr. Finley is a well known author and educator, having formerly been Professor of Politics at Princeton University, President of the College of the City of New York and Exchange Harvard Professor to the Sorbonne.

All members of the College, physicians of New York and visitors attending the Session, with their families, are cordially invited. Tickets should be purchased at the Registration Bureau by Wednesday afternoon.

PROGRAM OF ENTERTAINMENT FOR VISITING WOMEN

The Headquarters of the Women's Entertainment Committee will be located in the Empire Room at the Waldorf-Astoria Hotel. Each visitor will receive a program of the activities planned for their entertainment by the Women's Entertainment Committee. A special secretary will be in charge to assist visitors in arranging their entertainment program. Visiting women are requested to register here on arrival and make reservations for the events announced in the program. Additional literature containing information regarding theaters, restaurants, night clubs and other places of entertainment will be available at the registration desk.

The sole purpose of the Women's Entertainment Committee is to assist the visiting women in securing the greatest possible enjoyment and entertainment from their visit to New York. It is hoped that as a result of the activities of this Committee visitors will carry away with them pleasant memories of their stay.

It would greatly facilitate the work of the Committee if each Fellow or Associate who will be attended by ladies will return the card accompanying the program as promptly as possible.

Monday, April 4, 1938

Afternoon: Registration, Empire Room, Waldorf-Astoria Hotel.
Evening: 8:15 p.m., Reception in Empire Room.
9:00 p.m., Evening performance at Radio City Music Hall. Feature picture and stage show, including the famous Rockettes.

Tuesday, April 5, 1938

Morning: Free for shopping, etc.
Afternoon: 12:30 p.m., Luncheon and fashion show in the Empire Room. Tickets, $2.00.
Evening: Theater, optional.

Wednesday, April 6, 1938

Morning: Free.
Afternoon: 2:30 p.m., Visit to the Frick Museum and Metropolitan Museum of Art. Buses leave the Waldorf-Astoria at 2:30 p.m. Fare, $1.00.
5:00 p.m., Tea at the Junior League Club House as guests of the Women's Committee.
Evening: 8:30 p.m., Convocation and dance at the Waldorf-Astoria.

Thursday, April 7, 1938

Morning: 11:15 a.m., Tour of Radio City, including the Museum of Science and Industry, Sky Gardens, Broadcasting Studios, etc. Tickets, $1.50. Tour ends at 4:00 p.m. Luncheon may be had in restaurants in Radio City.
Evening: 8:00 p.m., Annual Banquet of the College, Waldorf-Astoria.

THE NEW YORK ACADEMY OF MEDICINE at 2 East 103rd Street (on Fifth Avenue) will be open to the members of the American College of Physicians and the participants in its Sessions in New York City.

The Library of the Academy of Medicine is open daily from 9:00 a.m. to 10:30 p.m. The Medical Library is the second largest in the United States, being excelled only by that of the Surgeon General's Library in Washington. The rare books and the Library's incunabula are particularly noteworthy.

The services of the Committee on Medical Education will be available to the members of the American College of Physicians and to all other visiting physicians for information relative to hospitals and clinics throughout the City of New York. The Committee also publishes a daily schedule and bulletin of medical and surgical meetings, lectures, conferences and rounds, as well as a daily list of major surgery in the city's hospitals, open to physicians.

On Friday evening, April 8, at eight-thirty o'clock, Dr. Thomas M. Rivers of the Rockefeller Institute will deliver the Biggs Memorial Lecture at the Academy upon the subject, "The Twentieth Century Version of the De Novo Origin of Infectious Agents, and its Significance in the Control of Disease." All members of the College who remain in New York that evening are cordially invited to attend this meeting.

THE AMERICAN MUSEUM OF NATURAL HISTORY at 77th Street from Columbus Avenue to Central Park West is open every day in the year: weekdays, including holidays, from 9:00 a.m. to 5:00 p.m., and Sundays from 1:00 p.m. to 5:00 p.m. There is no charge for admission, excepting to the Planetarium.

The Museum is an institution devoted to the study of the earth and the life existing on it, step by step over a period estimated to be over five hundred million years, from the lowest form to man. Here the fruits of more than half a century of scientific discovery, painstaking research, extensive exploration and courageous pioneering appear in the form of exhibits which reconstruct much of the history of the earth and the mighty animals that once roamed its surface. In the Museum's halls you will find thousands of natural history exhibits from virtually every section of the globe, aside from the special exhibits in the Roosevelt Memorial and the Hayden Planetarium.

THE EXPOSITION AND TECHNICAL EXHIBIT will be located on the Third Floor of the Waldorf-Astoria Hotel.

By official action of the Board of Regents of the College, the Technical Exhibits will be raised to a higher level of excellence through the elimination of all irrelevant and non-scientific entries. The rules adopted, governing this and future Exhibits, are as follows:

(1) Exhibitors shall be admitted on invitation only;

(2) The initial approved "Invitation List" shall be made up by the Committee and the Executive Secretary. Both the firm and the product must be approved. Preference shall be given to exhibits of a scientific nature, such as pharmaceuticals, equipment and medical books;

(3) Additions to the initial approved "Invitation List" may be made by the Committee after application by firms, with the requirement that they submit complete literature concerning their products and their organization;

(4) The "Invitation List" may be revised annually on the recommendation of the Committee.

The Committee on Exhibits has thoughtfully investigated each exhibit before extending invitations. The number of exhibitors has been reduced, and it is hoped that the members and visiting physicians will find the exhibits more interesting and more beneficial. The exhibits will be particularly representative of the interests of Internal Medicine and its allied specialties, and will include medical literature, pharmaceutical products, apparatus and appliances, specialized physicians' furniture and many other items of special interest. The educational value of these exhibits adds greatly to the interesting features of the meeting. Each doctor is urged to visit each of the booths, for he will certainly find something new and scientifically valuable. Special intermissions in the general program have been arranged, providing additional time for the inspection of exhibits.

LIST OF EXHIBITORS

The following exhibitors have been approved for admission to the Exhibit:

	Space
Adlanco X-Ray Corporation, New York, N. Y.	47–48
Allergia Products Co., Newton, Mass.	28
Allison Company, W. D., Indianapolis, Ind.	53
American Hospital Supply Corporation, Chicago, Ill.	15
Appleton-Century Company, D., New York, N. Y.	24
Arlington Chemical Company, The, Yonkers, N. Y.	2
Austin, Nichols & Co., Inc., Brooklyn, N. Y.	37
Ayerst, McKenna & Harrison (United States) Limited, Montreal, Que.	9
Baum Co., Inc., W. A., New York, N. Y.	55
Becton, Dickinson & Co., Rutherford, N. J.	72–73
Bilhuber-Knoll Corp., Jersey City, N. J.	25
Cambridge Instrument Co., Inc., New York, N. Y.	61
Cameron Surgical Specialty Company, Chicago, Ill.	21–59
Chappel Laboratories, Rockford, Ill.	14
Collins, Inc., Warren E., Boston, Mass.	54
Davies, Rose & Company, Limited, Boston, Mass.	7
Davis Company, F. A., Philadelphia, Pa.	30
Doak Company, The, Cleveland, Ohio	16
Fougera and Co., Inc., E., New York, N. Y.	26
General Electric X-Ray Corporation, Chicago, Ill.	33–34
Gerber Products Company, Fremont, Mich.	40
Glen Springs, The, Watkins Glen, N. Y.	45
Gradwohl School of Laboratory Technique, St. Louis, Mo.	32
Hamilton Manufacturing Co., Two Rivers, Wis.	41–42
Hoeber, Inc., Paul B., New York, N. Y.	27
Hoffmann-La Roche, Inc., Nutley, N. J.	44
Jones Metabolism Equipment Co., Chicago, Ill.	6
Kalak Water Co., New York, N. Y.	4
LaMotte Chemical Products Company, Baltimore, Md.	58
Lea & Febiger, Philadelphia, Pa.	20
Lederle Laboratories, Inc., New York, N. Y.	10–11–12
Lippincott Company, J. B., Philadelphia, Pa.	1
Macmillan Company, The, New York, N. Y.	60
Maltine Company, The, New York, N. Y.	74
Mead Johnson & Company, Inc., Evansville, Ind.	22
Medical Bureau, The, Chicago, Ill.	17
Medical Case History Bureau, New York, N. Y.	69
Merck & Co. Inc., Rahway, N. J.	18–19
Merrell Company, The Wm. S., Cincinnati, Ohio	68
Mosby Company, The C. V., St. Louis, Mo.	29
Muller Laboratories, The, Baltimore, Md.	56
Nelson & Sons, Thomas, New York, N. Y.	5
New York Medical Exchange, The, New York, N. Y.	3
Oxford University Press, New York, N. Y.	8
Oxygen Therapy Service, Inc., New York, N. Y.	57
Patch Company, The E. L., Boston, Mass.	23
Petrolagar Laboratories, Inc., Chicago, Ill.	70
Picker X-Ray Corporation, New York, N. Y.	35
Ralston Purina Co., St. Louis, Mo.	31
Rare Chemicals, Inc., Nepera Park, N. Y.	66–67

GENERAL SESSIONS

The object of the General Sessions portion of our program is to provide opportunity for the physicians who constitute our membership, and their guests, to hear statements by competent authorities on topics of lively interest in the fields of internal medicine, the basic sciences, related specialties and other fields in which knowledge gained will better fit the physician to serve the public and practice his profession.

The attempt has been made to provide a diversified and well balanced program. Reports of new and original work are included as well as reviews of important subjects. The desires of the membership as to both topics and speakers have been obtained insofar as this can be done by questionnaire, and heeded in the formation of the program.

In the belief that it is not incumbent upon the physician "to stick to his last" in a meeting of his College, if by that is meant that nothing but purely scientific medicine should he be permitted to consider, certain items touching upon *social, public* and possibly even *philosophical aspects* of medicine, as well as the more usual ones on diagnosis and treatment, have been included.

GENERAL SESSIONS PROGRAM

Ballroom, Waldorf-Astoria Hotel, New York, N. Y.

FIRST GENERAL SESSION

Monday Afternoon, April 4, 1938

Presiding Officer

James Alexander Miller, New York, N. Y.

p.m.
2:30 Addresses of Welcome:

James Alexander Miller, General Chairman of the Twenty-Second Annual Session, and President of the New York Academy of Medicine.

Clarence G. Bandler, President of the New York County Medical Society.

Willard C. Rappleye, Dean, College of Physicians and Surgeons, Columbia University.

Hon. Fiorello H. LaGuardia, Mayor of the City of New York.

Response to Addresses of Welcome:

James H. Means, President of the American College of Physicians.

OUTLINE OF SESSION

TIME	MONDAY	TUESDAY		WEDNESDAY		THURSDAY		FRIDAY	
9:00 a.m. to 12:00 m.	Morning free. Registration, Exhibits, etc.	3d General Session		4th General Session		5th General Session		6th General Session	
12:30 p.m. to 2:00 p.m.	Luncheon	Round Table Luncheons		Round Table Luncheons		Round Table Luncheons		Round Table Luncheons	
2:30 p.m. to 5:00 p.m.	1st General Session	1st Clinical Session	2:30–4:30 1st Lecture Program	2d Clinical Session	2:30–4:30 2d Lecture Program	3d Clinical Session	2:30–4:30 3d Lecture Program	4th Clinical Session	2:30–4:30 4th Lecture Program
5:00 p.m. to 8:00 p.m.	Dinner	Dinner		Dinner					
8:00 p.m. to 10:00 p.m.	2d General Session followed by Smoker	Open		Convocation, followed by President's Reception		ANNUAL BANQUET			

3:15 Trends in Public Health.
Thomas Parran, Surgeon-General, U. S. Public Health Service, Washington, D. C.
3:45 INTERMISSION.
4:15 The Social Responsibilities of Medicine.
John P. Peters, John Slade Ely Professor of Medicine, Yale University School of Medicine, New Haven, Conn. (By invitation.)
4:45 A Broader View of Postmortem Examinations.
Alan Gregg, Director for Medical Sciences of the Rockefeller Foundation, New York, N. Y. (By invitation.)
5:15 ADJOURNMENT.

SECOND GENERAL SESSION

Monday Evening, April 4, 1938

Presiding Officer

William J. Kerr, San Francisco, Calif.

p.m.
8:00 The Mechanism of Heat Loss and Temperature Regulation.
Eugene F. Du Bois, Professor of Medicine, Cornell University Medical College; Medical Director, Russell Sage Institute of Pathology; Physician-in-Chief, New York Hospital; New York, N. Y.
8:20 Some Desirable Supplements to the Present Trends in Medical Investigation.
Roger I. Lee, Fellow, Harvard University, and Consultant in Internal Medicine; Boston, Mass.
8:40 Certain Limitations of Preventive Medicine.
Henry A. Christian, Hersey Professor of the Theory and Practice of Physic, Harvard University Medical School; Physician-in-Chief, Peter Bent Brigham Hospital; Boston, Mass.
9:00 Clinical and Experimental Observations on Focal Infection.
Russell L. Cecil, Professor of Clinical Medicine, Cornell University Medical College, New York, N. Y., and
D. Murray Angevine, Instructor in Pathology, Cornell University Medical College, New York, N. Y. (By invitation.)
9:20 The Ageing Process as a Medical-Social Problem.
George Morris Piersol, Professor of Medicine, University of Pennsylvania Graduate School of Medicine; Physician-in-Chief, Abington Memorial Hospital; Physician, University of Pennsylvania Graduate Hospital; Philadelphia, Pa., and
Edward L. Bortz, Associate Professor of Medicine, University of Pennsylvania Graduate School of Medicine; Chief of Medical Service B, The Lankenau Hospital; Philadelphia, Pa.
9:40 Nutritional Deficiency Disease.
George R. Minot, Professor of Medicine, Harvard University Medical School; Director, Thorndike Memorial Laboratory, Boston City Hospital; Boston, Mass.
10:00 ADJOURNMENT.

10:20 o'Clock

SMOKER

Ballroom, Waldorf-Astoria Hotel

An interesting and amusing program has been arranged. Admission by registration badge. Men only.

THIRD GENERAL SESSION

Tuesday Morning, April 5, 1938

Presiding Officer

James E. Paullin, Atlanta, Ga.

a.m.

9:00 Experimental Heart Disease.
George Edward Hall, Associate Professor, Department of Medical Research, University of Toronto, Toronto, Ont., Canada. (By invitation.)

9:20 Concerning the Association of Bronchial Asthma and Left Ventricular Failure and the Possible Ill Effects from the Use of Epinephrine, unless the Latter can be Excluded.
Fred M. Smith, Professor and Head of Department of Theory and Practice of Medicine, State University of Iowa College of Medicine; Physician-in-Chief, University Hospitals; Iowa City, Iowa.

9:40 Further Comments on Coronary Thrombosis.
James B. Herrick, Emeritus Professor of Medicine, Rush Medical College, Chicago, Ill.

10:00 Obesity and Hypertension: Clinical and Experimental Observations.
J. Edwin Wood, Jr., Professor of the Practice of Medicine, University of Virginia Department of Medicine, University, Va., and
James R. Cash, Professor of Pathology, University of Virginia Department of Medicine, University, Va. (By invitation.)

10:15 Climate, Mode of Life, and Heart Disease.
Paul D. White, Physician, Massachusetts General Hospital; Lecturer in Medicine, Harvard University Medical School; Boston, Mass.

10:30 INTERMISSION.

11:00 Physiologic Effects of Operation (Bilateral Resection of Splanchnic Nerves and First and Second Lumbar Ganglia) for Essential Hypertension.
Edgar V. Allen, Associate Professor of Medicine, University of Minnesota (Mayo Foundation); Head of Section in Division of Medicine, Mayo Clinic; Rochester, Minn., and
A. W. Adson, Professor of Neurosurgery, University of Minnesota (Mayo Foundation); Head of Section on Neurosurgery, Mayo Clinic; Rochester, Minn. (By invitation.)

11:20 Prophylaxis in Allergy.
Richard A. Kern, Professor of Clinical Medicine, University of Pennsylvania School of Medicine and Graduate School of Medicine; Chief of Allergy Section and Chief of Outpatient Department, Hospital of the University of Pennsylvania; Philadelphia, Pa.

11:40 Physiological Methods in the Diagnosis and Treatment of Asthma and Emphysema. (Moving Picture Demonstration.)
Alvan L. Barach, Assistant Professor of Clinical Medicine, Columbia University College of Physicians and Surgeons, New York, N. Y.

12:00 ADJOURNMENT.

FOURTH GENERAL SESSION

Wednesday Morning, April 6, 1938

Presiding Officer

G. Gill Richards, Salt Lake City, Utah

a.m.

9:00 Chronic Brucellosis (Undulant Fever): An Analytical Study of the Positive Reactors among School Children.
Fred E. Angle and William H. Algie, Department of Medicine, University of Kansas Hospitals; Attending Physicians to Bethany Methodist Hospital, Providence Hospital and St. Margaret's Hospital; Kansas City, Kan.

9:15 Prognosis and Treatment of Erysipelas.
John A. Toomey, Associate Professor of Pediatrics, Western Reserve University School of Medicine, Cleveland, Ohio.

9:35 The Value of Antitoxin in Scarlet Fever.
Francis G. Blake, Sterling Professor of Medicine, Yale University School of Medicine; Physician-in-Chief, New Haven Hospital; New Haven, Conn.

9:50 Factors Influencing the Incidence and Course of Otitis Media in Scarlet Fever.
Conrad Wesselhoeft, Associate Professor of Theory and Practice, Boston University School of Medicine; Associate in Communicable Diseases (Department of Pediatrics and School of Public Health), Harvard University Medical School; Boston, Mass.

10:10 The Present Status of Methods for the Prophylaxis of Acute Anterior Poliomyelitis.
John A. Kolmer, Professor of Medicine, Temple University School of Medicine; Director of the Research Institute of Cutaneous Medicine; Philadelphia, Pa.

10:30 INTERMISSION.

11:00 Observations on the Clinical Aspects, Complications and Treatment of Acute Upper Respiratory Tract Infections.
Arlie V. Bock, Henry K. Oliver Professor of Hygiene, Harvard University; Physician, Massachusetts General Hospital; Boston, Mass. (By invitation.)

11:15 The Affective Disorders in Medical Practice.
Thomas P. Sprunt, Associate in Medicine, Johns Hopkins University School of Medicine; Associate Professor of Medicine, University of Maryland School of Medicine; Baltimore, Md.

11:30 Experimental Observations on the Treatment of Hypertension.
Harry Goldblatt, Professor of Experimental Pathology and Associate Director of the Institute of Pathology, Western Reserve University School of Medicine, Cleveland, Ohio. (By invitation.)

11:50 Experiences with Insulins of Prolonged Activity in Ambulatory Patients.
H. Clare Shepardson, Associate Clinical Professor of Medicine, University of California Medical School, San Francisco, Calif., and
Richard D. Friedlander, Instructor in Medicine, University of California Medical School, San Francisco, Calif. (By invitation.)

12:00 ADJOURNMENT.

ANNUAL CONVOCATION

Wednesday Evening, April 6, 1938

8:30 o'Clock

Grand Ballroom, Waldorf-Astoria Hotel

All members of the profession and the general public are cordially invited. No special admission tickets will be required.

1. Address by the President of the College.
James Howard Means.
2. Presentation of newly-elected Fellows and recital of the Pledge.
George Morris Piersol, *Secretary General.*
3. Presentation of John Phillips Memorial Medal for 1937–38.
4. Announcement of Research Fellow of the College for 1938.
5. Convocational Oration: "Possibilities in Biological Engineering."
Karl T. Compton, President, Massachusetts Institute of Technology, Cambridge, Mass.

President's Reception

The Reception and Dance will follow immediately after the program. Newly-inducted Fellows should sign the Roster and secure their Fellowship Certificates during the Reception.

FIFTH GENERAL SESSION

Thursday Morning, April 7, 1938

Presiding Officer

William D. Stroud, Philadelphia, Pa.

a.m.

9:00 The Clinical Significance of Punctate Basophilia in the Erythrocyte.
Ernest H. Falconer, Clinical Professor of Medicine, University of California Medical School, San Francisco, Calif.

9:15 Macrocytic Anemias, other than Pernicious Anemia, Associated with Lesions of the Gastrointestinal Tract.
Cyrus C. Sturgis, Professor of Internal Medicine, University of Michigan Medical School; Director, Thomas Henry Simpson Memorial Institute for Medical Research; Director, Department of Internal Medicine, University Hospital; Ann Arbor, Mich.

9:35 Clinical and Hematological Review of Sprue based on the Study of 150 Cases.
Ramón M. Suárez, Associate Clinical Professor of Tropical Medicine, School of Tropical Medicine of Puerto Rico, San Juan, P. R.

9:55 The Challenge of Appendicitis.
Reginald Fitz, Wade Professor of Medicine, Boston University School of Medicine; Director, Evans Memorial; Boston, Mass.

10:15 Correlation of Clinical and Laboratory Data in Diseases of Lymph Nodes.
Raphael Isaacs, Associate Professor of Medicine, University of Michigan Medical School; Assistant Director, Thomas Henry Simpson Memorial Institute for Medical Research; Ann Arbor, Mich.

10:30 INTERMISSION.

11:00 Concerning the Acquired Resistance of Fixed Tissue Cells to Injury. (Lantern slides.)
William de B. MacNider, Kenan Research Professor of Pharmacology, and Dean, University of North Carolina School of Medicine, Chapel Hill, N. C.

11:30 ADJOURNMENT, to be followed by

ANNUAL BUSINESS MEETING

The Annual Business Meeting of the College will be held immediately after the last paper. All Masters and Fellows are urged to be present. An amendment to the By-Laws of the College is to be presented for consideration and adoption. Official reports from the Treasurer and Executive Secretary will be read; new Officers, Regents and Governors will be elected, and the President-Elect, Dr. William J. Kerr, will be inducted into office.

Thursday Evening, 8:00 o'Clock

Ballroom, Waldorf-Astoria Hotel

THE ANNUAL BANQUET OF THE COLLEGE

(Procure Tickets at the Registration Bureau)

Consult Special Banquet Program

Toastmaster: James Alexander Miller, New York, N. Y.
Address of the Evening: "Education in a Changing World." Hon. John H. Finley, LL.D., Associate Editor of the New York Times.

SIXTH GENERAL SESSION

Friday Morning, April 8, 1938

Presiding Officer

James D. Bruce, Ann Arbor, Mich.

a.m.

9:00 A Differential Classification of the Various Types of Colitis: Their Management.
J. Arnold Bargen, Associate Professor of Medicine, University of Minnesota (Mayo Foundation); Consultant in Medicine, Mayo Clinic; Rochester, Minn.

9:15 Hypoglycemia Following Encephalitis.
Jonathan C. Meakins, Professor of Medicine and Director of Department, McGill University Faculty of Medicine; Physician-in-Chief, Royal Victoria Hospital; Montreal, Que., Canada.

9:30 Basal Metabolism: The Practical Significance of the "Variability" as Distinguished from the "Constancy" of the Basal Metabolic Rate in Individuals and in Various Groups of Diseases.
Walter M. Boothby, Professor of Experimental Metabolism, University of Minnesota (Mayo Foundation); Head of Section for Metabolic Investigation, Mayo Clinic; Rochester, Minn.

9:50 Studies on the Pathologic Physiology of the Exophthalmos of Graves' Disease.
David Marine, Assistant Professor of Pathology, Columbia University College of Physicians and Surgeons; Director of Laboratories, Montefiore Hospital; New York, N. Y.

10:10 Experiences in Treating Exophthalmic Goiter in a Large Municipal Hospital.
Willard O. Thompson, Associate Clinical Professor of Medicine, Rush Medical College; Research Associate in Pathology, Cook County Hospital; Chicago, Ill.;
S. G. Taylor, III, Clinical Associate in Medicine, Rush Medical College, Chicago, Ill. (By invitation);
Karl A. Meyer, Associate Professor of Surgery, Northwestern University Medical School; Attending Surgeon and Medical Superintendent, Cook County Hospital; Chicago, Ill. (By invitation);
R. W. McNealy, Associate Professor of Surgery, Northwestern University Medical School; Attending Surgeon, Cook County Hospital; Chicago, Ill. (By invitation.)

10:30 INTERMISSION.

11:00 Cevitamic Acid: A Critical Analysis of Its Use in Clinical Medicine.
Irving S. Wright, Assistant Professor of Clinical Medicine, Columbia University, New York, N. Y.

11:20 Common Gastrointestinal Emergencies: Their Early Recognition and Treatment.
George B. Eusterman, Professor of Medicine, University of Minnesota (Mayo Foundation); Head of Section on Medicine, Mayo Clinic; Rochester, Minn.

11:40 Acute Disseminated Lupus Erythematosus—a Systemic Disease.
Edward Rose, Assistant Professor of Clinical Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pa., and
Donald M. Pillsbury, Assistant Professor of Dermatology and Syphilology, University of Pennsylvania School of Medicine, Philadelphia, Pa. (By invitation.)

12:00 ADJOURNMENT.

PROGRAM OF AFTERNOON LECTURES

This course of Afternoon Lectures is a feature of the program arranged at the request of a large number of members. The course is presented as an elective, as a whole or for individual days, in place of hospital clinics. The lectures will not conflict with the General Sessions or with the Round Table Luncheon-Conferences. The lectures will be presented daily, Tuesday to Friday, inclusive, from 2:30 to 4:30 p.m., in the Ballroom of the Waldorf-Astoria Hotel.

This year the attempt has been made to devote most of the lectures to problems in therapeutics. The newer drugs such as sulphanilamide, physical therapy, oxygen therapy and psychotherapy will be presented, and also papers on treatment of disturbances of sodium metabolism and of such diseases as hypertension and disorders of the liver.

The lectures will be open to all members and guests of the College.
Admission by regular registration badge.

Tuesday Afternoon, April 5, 1938

BALLROOM, WALDORF-ASTORIA HOTEL

Presiding Officer

Chauncey Warring Dowden, Louisville, Ky.

p.m.

2:30 Therapeutics of Liver Disease.

Albert M. Snell, Associate Professor of Medicine, University of Minnesota (Mayo Foundation); Head of a Section on Medicine, Mayo Clinic; Rochester, Minn., and

Jesse L. Bollman, Associate Professor of Experimental Pathology, University of Minnesota (Mayo Foundation); Associate in Division of Experimental Surgery and Pathology, Mayo Clinic; Rochester, Minn. (By invitation.)

3:30 Recent Advances in the Use of Drugs for Treatment of Bacterial Infections.

Eli Kennerly Marshall, Jr., Professor of Pharmacology and Experimental Therapeutics, The Johns Hopkins University School of Medicine, Baltimore, Md. (By invitation.)

4:30 ADJOURNMENT.

Wednesday Afternoon, April 6, 1938

BALLROOM, WALDORF-ASTORIA HOTEL

Presiding Officer

T. Homer Coffen, Portland, Oregon

p.m.

2:30 Recent Advances in the Therapeutic Use of Drugs Whose Action Simulates Sympathetic and Parasympathetic Nervous Activity.

Isaac Starr, Hartzell Professor of Research Therapeutics, University of Pennsylvania School of Medicine, Philadelphia, Pa. (By invitation.)

3:30 A Critical Survey of Physical Therapy Technic.

Stafford L. Warren, Associate Professor of Medicine in Charge of Division of Radiology of the University of Rochester, School of Medicine and Dentistry, and Strong Memorial Hospital, Rochester, N. Y. (By invitation.)

4:30 ADJOURNMENT.

Thursday Afternoon, April 7, 1938

BALLROOM, WALDORF-ASTORIA HOTEL

Presiding Officer

Edward Leo Tuohy, Duluth, Minn.

p.m.

2:30 Treatment of Disturbances of Sodium Metabolism.

Dana W. Atchley, Associate Professor of Medicine, Columbia University College of Physicians and Surgeons, New York, N. Y. (By invitation.)

3:10 Sensitization Tests—Then What?
George L. Waldbott, Detroit, Mich.

3:50 The Emergency Treatment of Dangerous Hypertension.
Albert S. Hyman, Director, Witkin Foundation for the Study and Prevention of Heart Disease, New York, N. Y.

4:05 Typhus Fever (Brill's Disease). A Study of 271 Cases.
Simon Risefeld Blatteis, Clinical Professor of Medicine, New York University College of Medicine; Professor of Clinical Medicine, Long Island College of Medicine; Brooklyn, N. Y.

4:30 ADJOURNMENT.

Friday Afternoon, April 8, 1938

BALLROOM, WALDORF-ASTORIA HOTEL

Presiding Officer

Edwin Wagner Gehring, Portland, Maine

p.m.

2:30 Psychotherapy, with Special Reference to the Use of Hypnosis.
James L. McCartney, Psychiatrist, New York State Vocational Institution, Catskill, N. Y.

3:30 Oxygen Therapy.
Alex. M. Burgess, Chairman of Division of University Health and Assistant Professor of Biology, Brown University; Physician-in-Chief, Charles V. Chapin Hospital; Visiting Physician, Rhode Island Hospital; Providence, R. I.

4:30 ADJOURNMENT.

ROUND TABLES

The Round Tables proved so popular at the St. Louis meeting that they have been made a special feature of the New York program. They will be conducted by outstanding authorities on the subjects assigned.

All Round Tables are held at the Waldorf-Astoria Hotel, and *all* will be luncheon meetings. The groups will meet around the luncheon table beginning promptly at 12:30 p.m. and terminating promptly at 2:00 p.m. Being held at this time, there will be no conflict with the General Sessions in the forenoon and the Clinics in the afternoon.

Admission to these discussions will, of necessity, be limited by the seating capacity of the rooms in which they are held. There are rooms with a seating capacity for luncheon varying from 75 to 200 persons. A total of 625 can be accommodated each day. This means a total capacity of 2,500 persons for the session. This should provide accommodations for at least one Round Table Luncheon for every member of the College attending the Convention. Admission is by ticket only. Tickets are $1.75 each, which includes the cost of the luncheon, city and federal taxes and gratuities.

In order to insure reservations for the Round Tables, it will be necessary to make application promptly when the application forms are received with the formal program later. When the application is made it is suggested that the applicant submit in writing any question or phase of the subject which he wishes discussed. These requests will be considered by the Leaders of the Round Tables who will discuss such subjects as seem most in demand.

ROUND TABLE LUNCHEON-CONFERENCES

Room	Le Perroquet Suite	Jansen Suite Dining Room	Jansen Suite Salon	Assembly Rooms M to R	West Foyer
Capacity	150	75	100	100	200
Tuesday April 5	I DIABETES Russell M. Wilder Leader	II SYPHILIS Thomas Parran Leader	III TUBERCULOSIS Gerald B. Webb Leader	IV GASTRO-ENTEROLOGY T. Grier Miller Leader	V CARDIOLOGY Paul D. White Leader
Wednesday April 6	VI ALLERGY Robert A. Cooke Leader	VII VASCULAR DISEASE Eugene M. Landis Leader	VIII NUTRITION William P. Murphy Leader	IX PSYCHONEUROSES Austen Fox Riggs Leader	X ENDOCRINOLOGY David P. Barr Leader
Thursday April 7	XI PNEUMONIA Russell L. Cecil Leader	XII ARTHRITIS Ralph H. Boots Leader	XIII CARDIOLOGY Robert L. Levy Leader	XIV DIABETES H. O. Mosenthal Leader	XV DISEASES OF THE BLOOD George R. Minot Leader
Friday April 8	XVI ALLERGY Francis M. Rackemann Leader	XVII TUBERCULOSIS J. Burns Amberson, Jr. Leader	XVIII GASTRO-ENTEROLOGY George B. Eusterman Leader	XIX DISEASES OF THE BLOOD Cyrus C. Sturgis Leader	XX VIRUS DISEASES Thomas Francis, Jr. Leader

PROGRAM OF ROUND TABLES

Tuesday, April 5, 1938

WALDORF–ASTORIA HOTEL

Le Perroquet Suite, Fourth Floor

(Capacity, 150)

I

12:30–2:00 p.m. ROUND TABLE on Diabetes Mellitus.

Leader: Russell M. Wilder, Professor and Chief of Department of Medicine, University of Minnesota (Mayo Foundation); Consulting Physician, Mayo Clinic; Rochester, Minn.

WALDORF–ASTORIA HOTEL

Jansen Suite Dining Room, Fourth Floor

(Capacity, 75)

II

12:30–2:00 p.m. ROUND TABLE on Syphilis.

Leader: Thomas Parran, Surgeon-General, United States Public Health Service, Washington, D. C.

WALDORF–ASTORIA HOTEL

Jansen Suite Salon, Fourth Floor

(Capacity, 100)

III

12:30–2:00 p.m. ROUND TABLE on Tuberculosis.

Leader: Gerald B. Webb, Consulting Physician, Sunnyrest Sanatorium, Glockner Sanatorium and Hospital, National Methodist Episcopal Sanatorium for Tuberculosis and St. Francis Hospital and Sanatorium; President, Colorado Foundation for Research in Tuberculosis; Colorado Springs, Colo.

WALDORF–ASTORIA HOTEL

Assembly Rooms M to R, Fourth Floor

(Capacity, 100)

IV

12:30–2:00 p.m. ROUND TABLE on Gastro-Enterology.

Leader: T. Grier Miller, Professor of Clinical Medicine, University of Pennsylvania School of Medicine; Chief of Gastrointestinal Section, Hospital of the University of Pennsylvania; Philadelphia, Pa.

WALDORF-ASTORIA HOTEL

West Foyer, Third Floor

(Capacity, 200)

V

12:30–2:00 p.m. ROUND TABLE on Cardiology.

Leader: Paul D. White, Physician, Massachusetts General Hospital; Lecturer in Medicine, Harvard University Medical School; Boston, Mass.

Wednesday, April 6, 1938

WALDORF-ASTORIA HOTEL

Le Perroquet Suite, Fourth Floor

(Capacity, 150)

VI

12:30–2:00 p.m. ROUND TABLE on Diseases of Allergy.

Leader: Robert A. Cooke, Assistant Professor of Clinical Medicine, Cornell University Medical College; Special Consultant in Allergy and Director of Department of Allergy, Roosevelt Hospital; New York, N. Y.

WALDORF-ASTORIA HOTEL

Jansen Suite Dining Room, Fourth Floor

(Capacity, 75)

VII

12:30–2:00 p.m. ROUND TABLE on Vascular Disease.

Leader: Eugene M. Landis, Assistant Professor of Medicine and Research Associate in Pharmacology, University of Pennsylvania School of Medicine, Philadelphia, Pa.

WALDORF-ASTORIA HOTEL

Jansen Suite Salon, Fourth Floor

(Capacity, 100)

VIII

12:30–2:00 p.m. ROUND TABLE on Disorders of Nutrition.

Leader: William P. Murphy, Associate in Medicine, Harvard University Medical School; Senior Associate in Medicine, Peter Bent Brigham Hospital; Boston, Mass.

WALDORF-ASTORIA HOTEL

Assembly Rooms M to R, Fourth Floor

(Capacity, 100)

IX

12:30–2:00 p.m. ROUND TABLE on Psychoneuroses.

Leader: Austen Fox Riggs, Clinical Professor of Neurology, Columbia Uni-

versity College of Physicians and Surgeons; Medical Director and President of Austen Riggs Foundation; Stockbridge, Mass.

WALDORF-ASTORIA HOTEL

West Foyer, Third Floor

(Capacity, 200)

X

12:30–2:00 p.m. ROUND TABLE on Endocrinology.

Leader: David P. Barr, Professor of Medicine, Washington University School of Medicine; Physician-in-Chief, Barnes Hospital; St. Louis, Mo.

Thursday, April 7, 1938

WALDORF-ASTORIA HOTEL

Le Perroquet Suite, Fourth Floor

(Capacity, 150)

XI

12:30–2:00 p.m. ROUND TABLE on Pneumonia.

Leader: Russell L. Cecil, Professor of Clinical Medicine, Cornell University Medical College; Associate Visiting Physician, New York Hospital; New York, N. Y.

WALDORF-ASTORIA HOTEL

Jansen Suite Dining Room, Fourth Floor

(Capacity, 75)

XII

12:30–2:00 p.m. ROUND TABLE on Arthritis.

Leader: Ralph H. Boots, Associate in Medicine, Columbia University College of Physicians and Surgeons; Assistant Attending Physician and Physician to Arthritis Clinic, Presbyterian Hospital; New York, N. Y.

WALDORF-ASTORIA HOTEL

Jansen Suite Salon, Fourth Floor

(Capacity, 100)

XIII

12:30–2:00 p.m. ROUND TABLE on Cardiology.

Leader: Robert L. Levy, Professor of Clinical Medicine, Columbia University College of Physicians and Surgeons; Associate Visiting Physician and Cardiologist, Presbyterian Hospital; New York, N. Y.

WALDORF–ASTORIA HOTEL

Assembly Rooms M to R, Fourth Floor

(Capacity, 100)

XIV

12:30–2:00 p.m. ROUND TABLE on Diabetes Mellitus.

Leader: H. O. Mosenthal, Professor of Medicine, New York Post-Graduate Medical School, Columbia University; Attending Physician, New York Post-Graduate Hospital; New York, N. Y.

WALDORF–ASTORIA HOTEL

West Foyer, Third Floor

(Capacity, 200)

XV

12:30–2:00 p.m. ROUND TABLE on Diseases of the Blood.

Leader: George R. Minot, Professor of Medicine, Harvard University Medical School; Director, Thorndike Memorial Laboratory, Boston City Hospital; Boston, Mass.

Friday, April 8, 1938

WALDORF–ASTORIA HOTEL

Le Perroquet Suite, Fourth Floor

(Capacity, 150)

XVI

12:30–2:00 p.m. ROUND TABLE on Diseases of Allergy.

Leader: Francis M. Rackemann, Associate in Medicine, Harvard University Medical School; Physician and Chief of Medical Department, Massachusetts General Hospital; Boston, Mass.

WALDORF–ASTORIA HOTEL

Jansen Suite Dining Room, Fourth Floor

(Capacity, 75)

XVII

12:30–2:00 p.m. ROUND TABLE on Tuberculosis.

Leader: J. Burns Amberson, Jr., Professor of Clinical Medicine, Columbia University College of Physicians and Surgeons and New York University College of Medicine; Visiting Physician, Tuberculosis Service, Bellevue Hospital; New York, N. Y.

WALDORF-ASTORIA HOTEL

Jansen Suite Salon, Fourth Floor

(Capacity, 100)

XVIII

12:30–2:00 p.m. ROUND TABLE on Gastro-enterology.

Leader: George B. Eusterman, Professor of Medicine, University of Minnesota (Mayo Foundation); Head of Section on Medicine, Mayo Clinic; Rochester, Minn.

WALDORF-ASTORIA HOTEL

Assembly Rooms M to R, Fourth Floor

(Capacity, 100)

XIX

12:30–2:00 p.m. ROUND TABLE on Diseases of the Blood.

Leader: Cyrus C. Sturgis, Professor of Internal Medicine, University of Michigan Medical School; Director, Thomas Henry Simpson Memorial Institute for Medical Research; Director, Department of Internal Medicine, University Hospital; Ann Arbor, Mich.

WALDORF-ASTORIA HOTEL

West Foyer, Third Floor

(Capacity, 200)

XX

12:30–2:00 p.m. ROUND TABLE on Virus Diseases

Leader: Thomas Francis, Jr., Member of the Staff of the International Health Division of the Rockefeller Foundation, New York, N. Y.

PROGRAM OF CLINICS AND SPECIAL DEMONSTRATIONS

The Program for the Clinical Sessions has been completed, and, following an old New York custom, clinics will be held in the afternoon instead of in the morning.

There will be three separate clinics on each of the four days at Bellevue, New York and Presbyterian Hospitals. At Mount Sinai there will be two programs each day. The Department of Health is giving one clinic on each of the four days. The Hospital of the Rockefeller Institute is giving two programs during the week and the following hospitals are each offering one program on one afternoon: Roosevelt, St. Luke's, Long Island College and Post-Graduate.

All these clinics are to be patient-clinics, not lectures, and special effort has been made to have each clinic a sort of symposium dealing with the clinical phases of some one particular branch of medicine such as cardiac, vitamin, endocrine, renal or blood diseases. As a matter of fact, all the fields of medicine seem to be fairly well covered in the programs outlined.

Stress has also been laid on the Clinical Pathological Conferences and one or more of these will be found on each of the afternoons. Some of the clinics belong

in the group of general medicine in which the run-of-the-ward cases will be presented and discussed by the attending staff. This makes it possible to do away with the ward walks which had to be limited to very small groups.

The clinics to be given by the Department of Health draw the material from their very large clinics on syphilis and gonorrhea and deal with these important subjects, not only from the standpoint of diagnosis and therapy, but also from their public health and preventive aspects.

Of course, it has not been possible to utilize all of the vast facilities that New York affords nor to avail ourselves of the opportunities that were offered by many of the other hospitals and institutions in the city. It did not seem wise to provide seating capacity in excess of that demanded by the College for such sessions; the clinics as offered will accommodate 2,500 individuals daily.

Clinic Sessions will begin promptly at 2.30 o'clock in the afternoon. *Everyone who wishes to attend a clinic must secure a ticket, for the collection of tickets will be rigidly enforced.*

There will also be a few special demonstrations for relatively small groups. Those who are interested will have an opportunity to see Dr. Barach's oxygen and helium apparatus in practical use at the Presbyterian Hospital where Dr. Francis Carter Wood will also demonstrate the high voltage (1,000,000 volts) x-ray machine recently installed in the hospital.

At Mount Sinai Hospital Dr. Robert Frank will demonstrate his method of assaying sex hormones, and Dr. Reuben Ottenberg and his associates will demonstrate technical methods for studying liver function.

At Bellevue Dr. Howard Fox will have a small clinic for the demonstration of some especially interesting cases of cutaneous syphilis and Dr. Lucy Sutton will exhibit apparatus for fever therapy in children.

At New York Hospital Dr. Henry Richardson and his associates will give a special demonstration on various aspects of bronchiectasis and Dr. Eugene Du Bois will show his new metabolism unit for research purposes.

It will be noted that many of these demonstrations occupy only a relatively small portion of the time allotted to clinic sessions in an afternoon. It has been arranged that Fellows desiring to attend these short demonstrations may attend any of the other clinics that are in progress at the same hospital during the remainder of the afternoon, either before or after the demonstration. In this way they will not sacrifice an entire afternoon for a relatively short demonstration.

The Committee responsible for the assembling of these clinics has received the cordial coöperation of the staffs in the hospitals contributing and trusts that the program will meet with the hearty approval of the Fellows of the College.

NEW YORK CITY AS A MEDICAL CENTER

Historical Retrospect

Dr. James J. Walsh, author of "The History of Medicine in New York State," is authority for the statement that the history of medicine began when the first permanent colonists located at Fort Orange in 1625. There arrived two "consolers of the sick," Bastiaen Jansen Crol and Jan Huyck, who also conducted religious services until the arrival of the first ordained minister in 1628. In 1633 a second minister arrived, accompanied by a schoolmaster. Both added to the medical resources, for it was the duty of the schoolmaster to assist the dominie as consoler of the sick as well as to serve as the teacher of youth.

Any retrospect of medicine in New York would require frequent references to the contributions made to the subject by Dr. Walsh, and fortunately we have been allowed the liberty, by that distinguished physician and author, of quoting freely from his works in this brief presentation.

"The first surgeon (chirurgeon) to settle in the province of New York," writes Dr. Walsh, "was Harmen Meyndertsen Van den Bogaert, who arrived in New Amsterdam in 1631, as the surgeon of the ship 'Eendracht.' He became surgeon to Fort Orange (now Albany), and was noted for his cordial relations with the Indians, but was a victim to their treachery. O'Callaghan, in his History of New Netherlands, gives the name of an English surgeon, William Beaton (chirurgeon to the ship 'William,' of London) who practiced in New Amsterdam. The landing of ship surgeons led the Council of New Amsterdam to request Dr. Johannes La Montagne to issue permits to those sufficiently expert in medicine and surgery to practice in the colony. He also had the additional duty of determining the fitness of the barber surgeons who wanted to practice here. Toner notes the jealousy among the barber surgeons, as well as their frequent lack of skill, and the constant necessity for legal regulation. Dr. La Montagne, a Huguenot from Holland in 1637, was the first regular graduate in medicine to practice in the province, having received his degree from the University of Leyden. He acted as schoolmaster as well as physician; had a seat in the Council; and was vice director in command of Fort Orange. Kiliaen Van Rensselater in 1642 engaged Abraham Staes to go to the colony as surgeon.

"The first medical book to be published in what is now the United States was Dr. John Jones's "Plain, Concise and Practical Remarks on the Treatment of Wounds and Fractures." The author was the surgeon-general of the Continental troops. Mumford, in his Surgical Memoirs, said:

'American surgeons must look back to John Jones of New York as the first of their eminent professional forebears.' Dr. Jones was a medical apprentice of Dr. Cadwalader, of Philadelphia, the best-known surgeon in the country at that time. Thence Jones went to London, to come under the influence of John Hunter and Percival Pott; and to Paris to study under Petit and Le Dran, considered the greatest surgical teachers of the time. After a period at Edinburgh under Monro, he returned to America to become surgeon to the American troops in the French and Indian War. When he volunteered his services to the colonies during the Revolution, he was appointed surgeon-general and proved just the man for the position. The Continentals had the advantage of the best surgery of the time. Cadwalader Colden was an eminent physician, who devoted more time to science, government and history than to medicine.

" The colonies generally were infested by quacks and medical charlatans, and newspapers were used to advertise their curealls. In 1753, a medical regulation act was passed which required that 'all the physicians, surgeons and apothecaries in the province are to be licensed by a board consisting of the four oldest members of his Majesty's Council, the judges of the Supreme Court, the representatives of the City and Assembly, our Mayor and Recorder for the time being, or any seven of them, with the assistance of two physicians and two surgeons by the majority of them elected. Until after examination and licensing no one shall practice. Examinations shall be public.'

" No bills for medical services were collectable unless the practitioner had a license. There were already complaints as to exorbitance of doctors' fees, so the bills of physicians were to be submitted to an examiner appointed for that purpose, before presentation to the patient. It has been estimated by Toner that at the time of the Revolution there were 3,500 physicians in the colonies, of whom only 400 held the degree of M.D. A list of thirty-five has been compiled for New York alone.

" New York was a pioneer in American medical education. According to Dr. David Hosack, the founder of the botanical gardens on the site of which Rockefeller Center has been built, the first effort at the formal teaching of medicine in this country was the private course in human anatomy offered in New York City by Dr. John Bard and Dr. Peter Middleton, probably before 1750. The first formal teaching of anatomy in this country, in connection with an organized educational institution, was a course of lectures given at King's College, now Columbia University, in 1763 by Dr. Samuel Clossey, a graduate of Trinity College, Dublin. Five years later, Dr. Peter Middleton and Dr. Samuel Bard, the son of Dr. John Bard, the first physician to practice dissection in America, established the medical department of King's College. This institution gave the first degree of Bachelor of Medicine in 1769. The first degree of Doctor of Medicine was bestowed in New York in 1770 on Robert Tucker, and the second in

1771 on Samuel Kissam. Dr. Samuel Bard, professor of the theory and practice of physics in New York, Mumford declares to have been the most eminent physician of his time with the single exception of Dr. Rush.

"During the Revolution, medical instruction was irregular. After the Revolution the Columbia school resumed its classes and suffered severely from the 'Doctors' Riot' which took place in 1788, because of popular opposition to dissection. No legal way of obtaining bodies for purposes of dissection existed. Resurrectionism, that is the surreptitious removal of the recently buried to the dissecting room, was a common practice. On Sunday, April 13, 1788, some boys saw a dissected arm hanging in a window of the medical school, and when they called attention to it, a crowd collected. Some of them forcibly entered the building and destroyed many anatomical preparations. On Monday morning, a crowd collected around the college, and the mayor attempted to soothe their feelings. In the afternoon, the crowd gathered around the jail in which the doctors and medical students had taken refuge because of threatened violence. Baron Steuben, of Revolutionary fame, tried to pacify the mob. They knocked him down, and so upset his dignity that he quite lost his temper, calling out to the mayor, 'Fire! Duane, fire!' and the militia, summoned for protection, fired, killing seven rioters and wounding many more. After this the mob dispersed.

"The New York riot led to the passage of a law, in 1789, that 'science might not be injured by preventing the dissection of proper subjects.' This law provided that 'when any offender shall be convicted of murder, arson or burglary for which he shall be sentenced to suffer death, the courts may at their discretion add to the judgment that the body of such offender shall be delivered to the surgeons for dissection.' This legal provision of the bodies of executed criminals proved utterly inadequate for teaching by dissection, and 'body snatching' continued.

"It was more than sixty years after the 'Doctors' Riot,' before a law (1854) was enacted by the New York legislature, granting unclaimed bodies for anatomical purposes. Many prominent physicians recalled, later in life, unearthing bodies from cemeteries on Long Island, when they were students, and smuggling them across the ferry. Dr. Hartwell, in his lecture on 'The Hindrances to Anatomical Study in the United States, Including a Special Record of the Struggles of Our Early Anatomical Teachers,' tells of incidents similar to the Doctors' Riot in other cities.

"The Medical School of Columbia College was united in 1814 with the College of Physicians and Surgeons in the City of New York which had been incorporated in 1807. Not for a number of years were these pioneer medical schools followed by others—the New York Medical College (1850); the short-lived Metropolitan Medical College (1857–62); the Homeopathic Medical College (1860); the Bellevue Hospital Medical College (1861); and the Eclectic Medical College (1865).

" The first medical college in the state outside of the metropolis was the College of Physicians and Surgeons of the Western District of the State of New York, established at Fairfield, in 1809. After incorporation in 1812, this College continued to function until 1840, having graduated 609 physicians. Geneva Medical College, established in 1835, and Albany Medical College, incorporated in 1838, continued to advance medical education. The number of medical colleges increased, until in 1882 there were 13, with 2,982 students, and property valued at more than $703,000. The first woman in the United States to receive the degree of Doctor of Medicine was Elizabeth Blackwell, who graduated from the Geneva Medical College in 1849. Fifteen years later, the New York Medical College for Women was incorporated, to be followed in 1866 by the Women's College of Physicians and Surgeons. At the present time (1936), there are in the state 9 medical colleges with 2,507 students enrolled.

" New York's priority in this country in the provision of postgraduate education for physicians is worth noting. Struggling practitioners of medicine who had received very limited medical education and were sincerely desirous of doing better professional work, could take several months from their practice and spend these at postgraduate study, to the decided advantage of themselves and their patients. The first of these graduate medical schools was the New York Polyclinic, founded in 1882 by Dr. John Allen Wyeth, himself a distinguished surgeon, one of the many progressive workers in surgery whom New York owes to the South. He had served with distinction in the Confederate army, and was looked upon as a leader in the profession. He is honored by a statue to him on the grounds of the capitol of Montgomery, Alabama, his native state. The postgraduate work in medicine that he initiated was taken up in other cities throughout the country and came to be a valued feature of American medical teaching.

" Dr. Valentine Seaman, at New York Hospital, was the pioneer in this country in the training of nurses. The inscription below his portrait in the hospital commemorates this: ' In 1798 he organized in the New York Hospital the first regular training school for nurses, from which other schools have since been established and extended their blessings throughout the country.' In 1872, Bellevue Hospital secured Nightingale nurses and thus introduced the modern trained nurse into America. Up to this time, the nurses at Bellevue were mainly women who had been sentenced to the workhouse, which constituted one part of Bellevue under the commissioner of charities and correction. After sobering up, they were transferred to the hospital as nurses, if they had had any experience in family nursing. When the Nightingale nurses came from London, these women stoned them and called them ' scabs ' and ' blacklegs,' imported from England to take the jobs of good Americans.

" Bellevue was about as insanitary as a hospital could possibly be. Its death rate was extremely high. Infection was always rife. Erysipelas

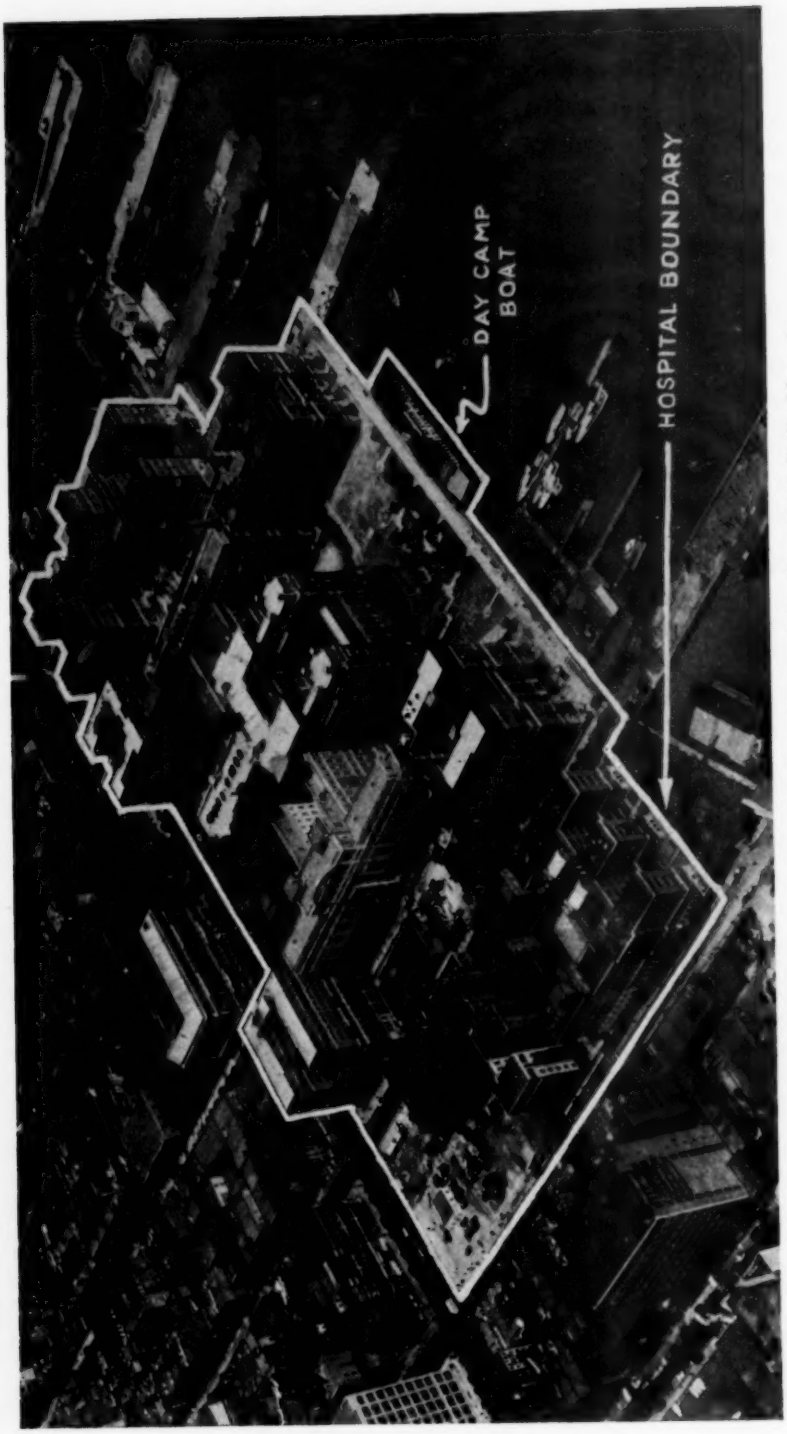

FIG. 1. Bellevue Hospital. (By permission of the New York Daily News.)

often proved fatal to surgical patients. No wonder the poor dreaded the hospital, though this was true of hospitals everywhere. It was almost worse to go to a hospital than to the poorhouse. Pasteur's discoveries in bacteriology, applied by Lister to surgery, reformed hospitals, though not until well toward the end of the nineteenth century. The trained nurse proved a valuable factor in this consummation so urgently needed."

Medicine in New York Today

New York City's opportunities for medical education are extensive. In all, there are 183 hospitals approved by the American Medical Association, with 837 approved internships available annually, and offering 396 annually available approved "residencies." Fifteen institutions offer post-graduate instruction.

Five medical schools are located in New York City: Columbia University College of Physicians and Surgeons, Cornell University Medical College, Long Island College of Medicine, New York Homeopathic College and Hospital, and New York University College of Medicine.

New York City is divided into five counties by boroughs: New York, Kings (Brooklyn), Queens, Bronx and Richmond (Staten Island). In each of these there is a county medical society which is an integral part of the Medical Society of the State of New York and the American Medical Association. Their membership comprises: New York, 4,755; Kings, 2,645; Queens, 809; Bronx, 1,247; and Richmond, 122.

The New York Academy of Medicine, at 2 East 103rd Street, Manhattan, was organized in 1847 and exists to advance medical knowledge. Its library is the second largest in the United States, containing 224,000 volumes. In Brooklyn, the Medical Society of the County of Kings has affiliated with it an Academy of Medicine at 1313 Bedford Avenue, Brooklyn, with a medical library ranking fourth in size in the country, containing 143,000 volumes. Both libraries contain many thousands of pamphlets and current medical journals available for reference.

During the course of the annual session, clinics and demonstrations will be held in the following hospitals: Bellevue, New York Hospital, Long Island College Hospital, St. Luke's, Roosevelt, Mt. Sinai, Presbyterian, and Post-Graduate Medical School and Hospital; also at the Rockefeller Institute for Medical Research and the Department of Health of New York City.

Bellevue Hospital. Bellevue Hospital is located at the foot of East 26th Street. It is the oldest hospital in the United States. Established in 1736, it was then known as the "Almshouse." In 1844 the teaching of medical students was begun and now the facilities of the hospital are utilized for teaching purposes by New York University, The College of Physicians and

Surgeons, Columbia University and by Cornell University Medical College. The Medical and Surgical Divisions are under the supervision of the Commissioner of Hospitals. The Training School for Nurses was opened in 1873. In 1887 a Training School for Male Nurses was begun. The present bed capacity is 2,431 and during 1938 the new Chest Building will be opened, adding an additional 360 beds. The hospital maintains a large Out-Patient Department and 612,378 patients' visits were cared for during the year 1937. The staff consists of a medical superintendent and assistant superintendents, 550 visiting physicians, 28 resident physicians, 198 interns and more than 1,000 nurses.

FIG. 2. New York Hospital—Cornell Medical Center.

New York Hospital. (York Avenue and 68th Street.) The Society of the New York Hospital was chartered in 1771 during the reign of George III, and during the Revolutionary War the hospital was used by the British. Since that time it has been a teaching hospital, and from 1912 its principal teaching affiliation has been with Cornell University Medical College. In 1932 the following institutions moved into the same group of buildings:

Society of the New York Hospital, Society of the Lying-In Hospital of the City of New York, Manhattan Maternity and Dispensary, New York Nursery and Child's Hospital, and Cornell University Medical College. The " New York Hospital—Cornell Medical College Association " is an informal committee which serves as a medium for coördinating the joint activities of the two institutions. Ground was broken for the Medical Center in 1929. The cost of the Center was approximately $15,000,000. The main building is twenty-six stories high.

Long Island College Hospital. (Henry and Pacific Streets, Brooklyn.) Founded in 1858, this was the first medical college in the United States to incorporate its own hospital.

FIG. 3. Long Island College Hospital.

The first course of lectures at the Medical School began on March 30, 1860. In this same year the number of hospital beds was increased to provide for the many sick and wounded soldiers of the Civil War. The Long Island College Hospital was the first hospital in the Metropolitan District to receive wounded soldiers for nursing and medical treatment. The Long Island College Hospital has grown from an infant institution of twenty-five beds, housed in a private dwelling, to a modern hospital of 486 beds, a modern laboratory, a nurses home and a clinic treating 123,819

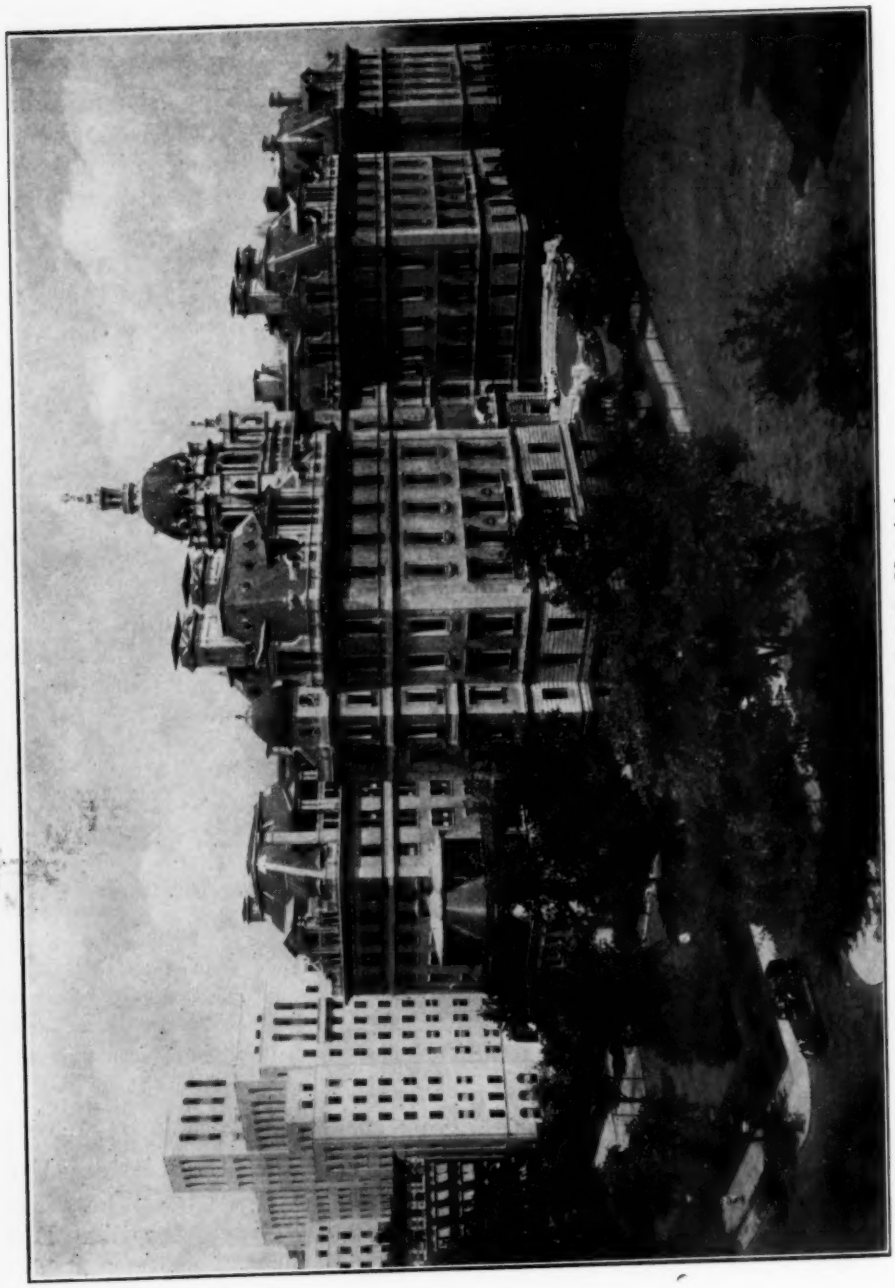

FIG. 4. St. Luke's Hospital.

patients a year. In 1930 the college and the hospital separated, the college changing its name to the Long Island College of Medicine. It still uses the hospital freely in teaching. The present hospital building is about thirty years old, while the Polhemus Memorial Clinic was built in 1896. The Hoagland Laboratory (1887), which was the first bacteriological laboratory built in the United States, and the Polak Laboratory (1931), are included in the group of buildings about the college.

St. Luke's Hospital. (Cathedral Heights, 113th Street and Amsterdam Avenue.) The hospital is open at all times for medical and surgical aid and nursing to the sick, and disabled from acute, curable, non-contagious

FIG. 5. Roosevelt Hospital.

diseases, without distinction of race or color. Cases demanding immediate care are received at any hour of the day or night. The hospital is supported by voluntary contributions and endowments. It is free to those unable to pay for services. St. Lukes also maintains a dispensary, training school for nurses and a hospital service.

Roosevelt Hospital. (Ninth Avenue and 59th Street.) Roosevelt Hospital was opened in 1871. It is a general hospital with 391 beds. In 1936

FIG. 6. Mt. Sinai Hospital.

there were 7,351 patients admitted and 66,085 visits were made to the Out-Patient Department. It is used for clinical teaching by the College of Physicians and Surgeons of Columbia University. A training school for nurses and an emergency department are conducted by the institution.

Mt. Sinai Hospital. (Fifth and Madison Avenues between 100th and 101st Streets.) Organized in 1852 for "benevolent, charitable and scientific purposes." The work of the hospital was begun in a small private dwelling on 28th Street between 7th and 8th Avenues. It accommodated 28 patients. The hospital now has accommodations for 856 patients, including eighteen beds in the Receiving Ward; 250,000 visits are made annually to its Out-Patient Clinic. Mt. Sinai created a precedent among the hospitals in New York in 1878 by setting up a distinct pediatric service, and

FIG. 7. Columbia-Presbyterian Medical Center.

an otological service in 1879. There is a training school for nurses in connection with Mt. Sinai, which was incorporated in 1881. The present hospital was completed and occupied March 15, 1904. Additions to the original group of buildings have been made continuously since that time. The Research Foundation of the Mt. Sinai Hospital was incorporated in 1936, "to conduct, promote, encourage and assist investigation in the services and arts of hygiene, medicine, surgery and allied subjects."

Presbyterian Hospital. Located with twelve other units composing the "Medical Center" at Broadway and 168th Street, it was founded in 1876, and is affiliated with the College of Physicians and Surgeons, the Medical

Department of Columbia University. The Hospital moved into the present buildings in 1928. On the present site are grouped, besides the Presbyterian Hospital and the College of Physicians and Surgeons of Columbia University, the Sloan Hospital for Women, the New York State Psychiatric Institute and Hospital, the Babies' Hospital, the Squier Urological Clinic, Presbyterian Hospital and Sloane Hospital Schools of Nursing, the Neurological Institute and Hospital, the Stephen V. Harkness Patient Pavilion, the School of Dental and Oral Surgery, the Vanderbilt Clinic, the Eye Institute, and the DeLamar Institute of Public Health. There are 1,674 beds.

FIG. 8. Buildings of the Rockefeller Institute for Medical Research, New York. The Laboratory Buildings are shown to the left. The Hospital Building and Isolation Building are at the right in the photograph.

The entire Medical Center, known as the Columbia-Presbyterian Medical Center, of which the Presbyterian Hospital is a part, covers twenty-two acres and cost $25,000,000.

Rockefeller Institute for Medical Research. (York Avenue and 68th Street.) The Hospital of The Rockefeller Institute for Medical Research was opened in 1910. The principles of organization of the Hospital were: first, that the number of diseases studied at any one time would be limited

and only patients suffering from one or another of the diseases under investigation would be accepted; second, that all the scientific staff was to devote its entire time to the duties of the Hospital; third, that the work of the Hospital staff should consist not merely in observational studies, but in experimental studies equally; and fourth, that no charge was to be exacted from the patients for services rendered. These principles have been strictly followed. The Hospital has 60 beds and an Out-Patient Department.

New York Post-Graduate Medical School and Hospital. Location: 30 East 20th Street. The oldest institution in this country engaged solely in the teaching of graduate medicine, having been founded in 1882. The School was incorporated into the educational system of Columbia University

FIG. 9. New York Post-Graduate Medical School and Hospital.

in January 1931 and registers more than five hundred physicians annually. The Hospital maintains 410 beds and an out-patient service notable for the variety and size of its clinics. There are two extramural units: the Reconstruction Hospital with 65 beds for accident cases and conditions arising out of industrial injury and disease; and the former New York Skin and Cancer Hospital now operated as an out-patient service for skin and cancer cases only, the in-patients being hospitalized in the main hospital building. Certain wards of the Metropolitan, Willard Parker and Sea View Hospitals, and the Hospital for Joint Diseases are also used for teaching purposes.

The *New York City Department of Health* operates seventeen clinics for the diagnosis of syphilis, gonorrhea, and lymphogranuloma inguinale. Ten of these clinics are also treatment centers. Annually, about 24,000 patients make over 400,000 visits to these clinics which conduct 120 sessions per week, serving all parts of the city. For the clinical demonstration arranged for the American College of Physicians, cases will be selected from these clinics and brought to the new Health Department Building at 125 Worth Street.